UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	)	CIVIL ACTION NO. 05-40048-FDS

MEMORANDUM IN SUPPORT OF PLAINTIFFS' MOTION TO FULLY INCLUDE THEIR CAUSATION EXPERTS' TESTIMONY AT TRIAL

Introduction

On May 16, 1994, Dan Allen, the popular and successful head football coach of The College of the Holy Cross, died from amyotrophic lateral sclerosis, known commonly as ALS or Lou Gehrig's disease.

Coach Allen's wife, Laura Allen, brought this wrongful death action on behalf of Coach Allen's estate and beneficiaries. She alleges that the defendants exposed Coach Allen to neurotoxic levels of Toluene, a chemical ingredient in materials used by defendants to re-surface the gymnasium floor in the same building which housed the offices of Coach Allen and his staff in May-June 2001. Plaintiffs assert that defendants were negligent in failing to properly warn Coach Allen and his staff of the dangerous propensities of the materials they were using, as well as the need to keep out of the building during the re-surfacing process. As a result, during the days and weeks in which the defendants' employees were working in an environment dangerous enough for them to wear respirator masks[1], Coach Allen and his staff daily and unknowingly exposed themselves to a known neurotoxin, Toluene[2].

Pursuant to FRE 702, Plaintiffs respectfully now move this Court to allow their experts to offer their causation opinions at trial.

At the outset of this motion, it is critical for the Court to understand this: it is NOT plaintiff's contention that Toluene causes ALS, or that Toluene caused Coach Allen to develop ALS. Rather, plaintiffs assert that Coach Allen was pre-disposed to developing ALS, and would likely have developed overt symptoms of, and died from

[1] See Affidavit of Martin Surfacing former employee Paul Crecilius, **Tab 14**.
[2] Indeed, defendant's own expert, Dr. Dean Hashimoto, testified at deposition it's a "truism" that Toluene is a neurotoxin at sufficient doses. Deposition of Dean Hashimoto, pages 55-56.

ALS, several years later in life, but because of his temporal exposure to neurotoxic levels of Toluene by defendants, Coach Allen's development of overt symptoms, and deadly course of ALS was accelerated by approximately five years of his life. This deprived Coach Allen of five meaningful years for him and his family, whose children were teenagers at the time their father was lost.

Plaintiffs have identified three well-qualified and respected experts in their respective fields to explain via proper scientific and medical process, how Coach Allen was exposed to the Toluene, how Toluene is a well-accepted neurotoxin capable of accelerating neurodegenerative disorders such as ALS, and how it did so in this case:

1. Marcia Ratner, Ph.D., is a well known and respected expert and educator in neurotoxins and their relation to neurodegenerative disease processes, with a unique clinical background in pharmacology, toxicology, neurology blended with an active bench/research science career (in which she investigates potential new drug compounds to treat neurodegenerative diseases including ALS). Dr. Ratner addresses Toluene's capability as a neurotoxin to hasten the course of the neurodegenerative disease ALS, and how it did so in this case. Her CV and report are at **Tabs 1**, **2a** (original report) **and 2b** (supplemental report);

2. Christine Oliver, MD, is an occupational medicine physician within the Harvard Medical system, and a private consultant. Dr. Oliver addresses Coach Allen's medical history, the Toluene exposure at the Field House, and the relation between Coach Allen's exposure to Toluene and his ALS onset. Her CV and report are at **Tabs 3** and **4**; and

3. William Ewing is an industrial hygienist; he explains the process by which the Holy Cross gym floor was re-surfaced and how the materials used, in particular Toluene, provided sufficient exposure levels to cause a neurotoxic reaction. His CV and report are at **Tabs 5** and **6**;

In addition, Plaintiffs have also disclosed an expert to assist the court in understanding the process of causal inference for purposes of this *Daubert* inquiry. Professor Richard Clapp is an internationally known and respected epidemiologist, with a focus on the causal relation between environmental toxins and disease, who regularly consults with

the federal bench on matters related to *Daubert* and causal inference, and teaches locally at Boston University's Department of Environmental Health. Dr. Clapp's CV is appended at **Tab 7**. His Rule 26 report is appended at **Tab 8**.[3]

Defendants, on the other hand, chose to disclose only one expert, Dr. Dean Hashimoto. Dr. Hashimoto is also an expert in his field of occupational medicine. However, in his initial Rule 26 disclosure (**Tab 9**), Dr. Hashimoto addresses an issue which has NO relevance to this inquiry: whether Toluene causes ALS. Plaintiffs agree with Dr. Hashimoto: it is NOT accepted that Toluene causes ALS. But that is not the issue here. The inquiry here is, **whether there is sufficient scientific evidence and explanation as to whether and how Toluene -- a neurotoxin -- is capable of accelerating the course of a neurodegenerative disease such as ALS, and whether it did so in the case of Coach Allen**. Dr. Hashimoto does not address this issue at all in his initial report and, even when given the opportunity to address it in his supplemental report (**Tab 10**), the defense expert barely touches on the subject (essentially only to say that, because there is insufficient evidence that toluene causes ALS, there is necessarily insufficient evidence to show that toluene can accelerate ALS). With due respect to Dr. Hashimoto, this particular question is not within the scope of his expertise: he is not a neurologist, toxicologist, pharmacologist or bench scientist.

As this Court will see, plaintiffs' causation experts satisfy the FRE 702/*Daubert* criteria and should be permitted to testify at trial.

[3] Plaintiffs have also disclosed an economist report to address damages, which is not at issue here; and moreover, defendants offer no report in rebuttal.

1. **Coach Allen's Exposure to Toluene; The Medical Chronology Leading to His Death; and An Overview of ALS**.

The reports of plaintiff experts Ratner, Oliver and Ewing, along with supporting documents cited therein[4], document the following:

As of May/June 2001, Coach Allen was the head coach of the football program at the College of the Holy Cross. He was 45 years old and in good physical health. There was no history of ALS in his family. In late May through early June, 2001, employees of the defendant Martin Surfacing re-surfaced the gym floor in the building known as the Field House at Holy Cross College. Coach Allen's office was located on the second floor of the Field House, and he was present throughout the course of the re-surfacing work. The workers performing the re-surfacing made use of several chemicals, all as listed on certain "Material Safety Data" (or "MSDS") sheets provided by defense counsel. These chemicals included Toluene. The refinishing process took at least one full workweek to complete.

During the refurbishment process, Coach Allen experienced acute symptoms of dizziness, headaches, and disorientation. Coach Allen's staff suffered similar acute symptoms. Plaintiff's experts have relied upon affidavits from three of Coach Allen's staff -- Bob Bradley, Larry Napolitano and Paul Bacchia -- who document Coach Allen's state of health and symptoms prior to, and during the re-surfacing. In addition, plaintiffs' experts rely upon an affidavit from one of the defendant's former employees, Paul Crecilius, who describes the re-surfacing process itself[5]. Those affidavits are attached here at **Tabs 11-14**. In addition, Coach Allen himself documented this incident before

[4] Including all available medical records, material safety data sheets, documents produced by the defendant and Holy Cross, deposition transcripts and the documents specifically identified below.
[5] As a reminder to the court, Martin Surfacing no longer exists; its parent company is bankrupt.

he died. Out of privacy concerns, his narrative has not been filed here, but will be provided to the Court upon request.

In the months after the re-surfacing, Coach Allen experienced symptoms of fatigue and weakness for which he sought medical consultation with his primary care physician and a neurologist. By September 2001, Coach Allen developed fasciculations (small, local, involuntary muscle contraction or twitching visible under the skin) in the lower extremities, which spread to the arms. He became wheelchair-bound in the spring of 2003. The neurologists treating Coach Allen diagnosed his condition as ALS. Coach Allen continued to suffer for one more year, passing on May 16, 2004.

Shortly before Coach Allen died, plaintiff expert Ratner and her colleague at Boston University, neurologist Dr. Joseph Jabre, had the important opportunity to conduct their own clinical neurological examination, and concurred in the diagnosis of ALS. Defendants' expert Hashimoto does not offer an alternative diagnosis.

Amyotrophic lateral sclerosis (ALS)

The National Institute of Neurological Disorders and Stroke (NINDS) defines ALS (sometimes called Lou Gehrig's disease) as a rapidly progressive, invariably fatal neurological disease that attacks the nerve cells *(neurons)* responsible for controlling voluntary muscles. In ALS, both the upper motor neurons and the lower motor neurons degenerate or die, ceasing to send messages to muscles. Unable to function, the muscles gradually weaken, waste away, and twitch. Eventually the ability of the brain to start and control voluntary movement is lost. Individuals with ALS lose their strength and the ability to move their arms, legs, and body. When muscles in the diaphragm and chest wall fail, individuals lose the ability to breathe without ventilatory support. The disease does

not affect a person's ability to see, smell, taste, hear, or recognize touch, and it does not usually impair a person's thinking or other cognitive abilities.

2. Causal Inference

Dr. Ratner's report (supported by Dr. Oliver) examines two "big picture" questions: (a) whether the neurotoxic chemicals to which Mr. Allen was exposed are capable of altering or hastening the course of a neurodegenerative disease like ALS (we can refer to this as "General Causation"); and (b) whether this exposure was at least a substantial contributing cause to hastening the course of Mr. Allen's ALS (we can refer to this as "Specific Causation").

As Drs. Ratner and Clapp describe in detail in their reports, General Causation in science is an inference, a judgment based upon observational and experimental deductions as well as an understanding of the general laws of nature. A single study is generally not sufficient for a causal inference. That is why the conclusions of most studies, no matter how large or small, speak in terms of their results "suggesting" that, for example, A is implicated in B. Published and peer-reviewed scientific studies almost never speak in language of "causation". So, as will be seen in Dr. Ratner's report, many studies are cited which make "suggestions" based upon well-designed and carried out methods. These studies, along with other methods of the scientific process, then form the basis for making a causal inference. Another way of thinking of the use of the word "suggests" when it appears in scientific literature is, "provides evidence in support of".

As a scientist, Dr. Ratner is obligated to consider all available scientific evidence in assessing a causal inference. That includes not only large epidemiologic case-control studies, but also the smallest experimental studies looking at a handful of rats (or even

just looking at molecules), or anecdotal reports of events occurring in a few persons, as well as the pharmacology, toxicology, biologically plausible theories and mechanisms of actions. The fact that a study has flaws or is not "statistically significant" does not mean the study should be disregarded; indeed, it is scientifically inappropriate to fail to consider the cumulative effect of all scientific evidence. In the real world, scientists and physicians infer causation from the totality of several lines of evidence that, together, comprise the body of existing scientific data. That is precisely what Dr. Ratner has done in this case. And what Dr. Hashimoto has failed to do.

Epidemiology

Because the centerpiece of the defense position appears to revolve around epidemiology, it is worth addressing the role of epidemiology in causal inference and in this case.

As Dr. Ratner explains in her report, epidemiology is generally and simply defined as the study of the patterns, causes and control of diseases in sample populations. When relevant epidemiology is available, it can be a useful tool and must be considered in a scientist's General Causation assessment. Epidemiology is not useful to assess so-called Specific Causation.

Many epidemiological studies have focused on elucidating the etiology of ALS, and therefore have asked whether chemicals "cause" or "trigger" the disease. Although numerous solvents and other industrial chemicals have neurotoxic properties, past exposure to these agents is often difficult to quantify and validate making these studies difficult to design and interpret.

Among the possible reasons for the paucity of data is the simple fact that the answer is intuitive as is discussed in detail by Dr. Ratner (i.e., if exposure to neurotoxicants kills neurons and ALS kills neurons then the additive effects of the two events occurring in the same individual should be a younger age at onset of the disease). Another reason is funding limitations; why spend money and time looking at factors that modify the clinical course of the disease when the more important question of what causes ALS has not yet been answered? Moreover, and importantly, the only entities with the financial means to conduct epidemiological studies to examine the role of a specific chemical in altering the course of ALS, is the chemical industry, and while industry has the means to conduct such a study, it does not have the motivation to do so, for obvious business reasons.

So, there is admittedly little epidemiologic data which is directly on point[6]; but, there are no epidemiologic studies which contradict the position taken by plaintiffs. It is often the case, when examining the neurotoxicity of chemicals, that there will be little to no epidemiology on point, and yet scientists are constantly able to arrive at sound and rational causal inferences, through the scientific method by examining all available scientific evidence, as Dr. Ratner done here.

As we proceed to the plaintiffs' experts' opinions, bear in mind that Dr. Hashimoto chose NOT to examine all the scientific evidence and also failed to address the real question here: is Toluene capable of accelerating the course of ALS, and did it do so in the case of Coach Allen? As Dr. Clapp observes in his report (**Tab 8**) at pages 11-12:

[6] For example, a peer-reviewed observational study published in May 2007 (addressed in Dr. Ratner's supplemental report (**Tab 2b**)) does support her explanation of the mechanisms by which Toluene is capable of accelerating ALS.

> In this matter, Dr. Dean Hashimoto has reviewed Mr. Dan Allen's medical history and the various epidemiologic studies listed in his report. He gives little attention to the studies regarding chemical exposures and the development of amyotrophic lateral sclerosis (ALS) and he notes the absence of a "statistically significant association" between solvents and ALS in some of the studies and concludes that it is more likely than not that Mr. Allen's disease was not caused by solvent exposure. Dr. Hashimoto does not discuss other important information biologic mechanisms of neurological damage from solvents, exposure-related symptoms Mr. Allen experienced at the time of the re-surfacing, and case reports of solvent-exposed individuals in the scientific literature. He has therefore failed to take into account the full range of relevant information that is available before reaching his conclusion.
> . . .
>
> The scientific method followed by Dr. Ratner detailed and comprehensive and therefore more appropriate in rendering her opinion than Dr. Hashimoto's method. She has considered and presented the full range of relevant information in forming her opinion.

3. Dr. Ratner's Opinion

Dr. Ratner's professional education, experience and training have created a unique combination of clinical, academic and laboratory-based expertise in the very subject matter at issue in this legal case: assessing the causal role of an exposure to neurotoxic chemicals to the onset of a neurodegenerative disease. There are few scientists in the country with this clinical/academic/bench-science background.

Most of Dr. Ratner's report delves into a good amount of scientific, pharmacological, and toxicological terminology and principles, which can be confusing or complicated for lay readers, but we have endeavored to explain her scientific bases as accurately and completely as possible. The following is a more digestible summary of the underlying basis for her General Causation opinion, that the chemicals to which Dan

Allen was exposed (and particularly Toluene) were capable of hastening the onset of his ALS.

1. While science does not know what causes ALS, science does understand, and it is generally accepted as to how ALS occurs; that is, science does understand the neuropathology and the mechanisms by which neurodegeneration occurs, and Dr. Ratner has described these mechanisms in her report.

2. The chemicals to which Dan Allen was exposed, and in particular Toluene, are known and generally accepted neurotoxicants; that is, they are toxic to, and can kill, human neurons.

3. Science also knows the mechanisms by which Toluene acts as a neurotoxicant, and this knowledge is also generally accepted; Dr. Ratner has described these mechanisms in her report.

4. The mechanisms by which neurodegeneration occurs in ALS are exactly the same mechanisms by which Toluene acts upon neurons.

5. Scientific logic therefore dictates that Toluene is capable of altering or hastening subclinical and clinical course of ALS since the interaction of the toxic effects of toluene with the neuropathological mechanisms implicated in ALS will result in an additive effect.

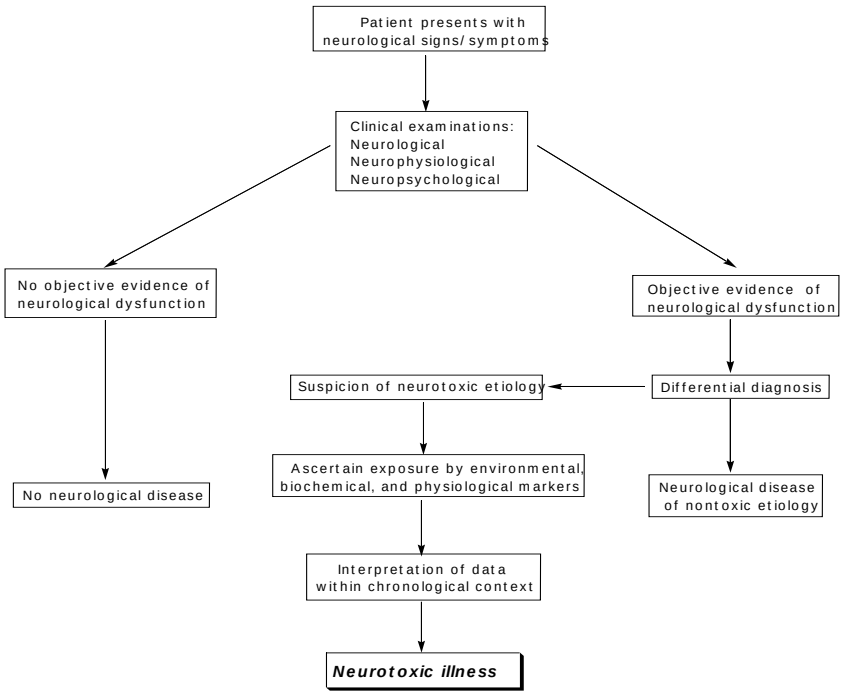
6. While few studies have looked at age at onset of ALS among subjects exposed to chemicals, many researchers have looked for chemicals that can slow the disease. The NINDS (National Institute of Neurological Disorders and Stroke) recognizes that the clinical course of the disease can be slowed by certain chemicals. The FDA has approved the first drug treatment for the disease, *Riluzole*. Riluzole is believed to reduce damage to motor neurons and prolongs survival by several months, mainly in those with difficulty swallowing.

7. If a chemical can be used as a pharmaceutical to extend survival in ALS, can exposure to a chemical also curtail survival (or in order words, hasten onset of ALS)? To answer this question Dr. Ratner identifies in her report putative points of interaction between the chemicals to which Mr. Allen was exposed in his workplace and the mechanisms of neurodegeneration implicated in ALS. For example, if oxidative stress is implicated in ALS and Mr. Allen was exposed to a chemical that increases oxidative stress, then plaintiffs have identified a putative point of interaction. Likewise, if increased glutamatergic neurotransmission is implicated in ALS and Mr. Allen was exposed to a chemical that increases glutamatergic neurotransmission, then we have identified another putative point of

> interaction. In fact, review of the literature on ALS and the Material Safety Data Sheets of the chemicals used by Martin Surfacing to perform the floor re-surfacing at issue, clearly demonstrates that these were two of the ways in which the exposures that occurred during the floor refinishing process interacted with the latent disease from which Coach Allen eventually died.

Dr. Ratner's report presents in tremendous detail, peer-reviewed scientific data supporting the conclusion that Coach Allen's exposure to Toluene and other compounds used in the floor refinishing process at Holy Cross accelerated his latent ALS and was at least a substantial contributing factor to the progression of his disease.

Just as there is an accepted method in assessing General Causation, so too, there is a generally accepted method in neurotoxicity cases to assess Specific Causation. Dr. Ratner helped to develop the diagnostic algorithm for this assessment. This method has been received by the scientific community and has been published in peer-reviewed journals without criticism. For example, Dr. Ratner and her mentor presented their model in the well-respected and peer-reviewed professional series, Neurologic Clinics in May 1999, in an article entitled, "Approach to Neurotoxicity Tort Cases". As it has now withstood the test of time for more than seven years, it can be considered generally accepted. This can be diagrammed as follows:



Dr. Ratner followed this generally accepted method for assessing Specific Causation in the case of Coach Allen to arrive at the following conclusions with a reasonable degree of scientific certainty:

1. Coach Allen and his coworkers reported exposures to chemicals at concentrations that were at least high enough to cause acute symptoms including dizziness, nausea and headaches. It can therefore be concluded that the exposures were high enough to alter neuronal functioning since dizziness is a symptom of this;

2. Mr. Allen developed symptoms of ALS in chronological relationship to this specific exposure event; and

3. Mr. Allen had no family history of ALS which typically develops earlier in life than sporadic ALS but also runs a slightly longer course. His first overt symptoms of ALS emerged when he was only 45-years-old. ALS is general considered to be a disease of middle to late life. Published reports indicate that the average age at onset for non-familial sporadic ALS is 60 years-old. These observations indicate that Mr. Allen developed the disease much earlier than would be expected based on his negative family history and the epidemiological findings; therefore

4. It can be concluded with a reasonable degree of medical certainty that Mr. Allen would have been unlikely to develop overt symptoms of ALS at age

45-years-old and would not have died on May 16, 2004 had he not been exposed to the chemicals used in the gym floor refurbishment process.

Finally, Dr. Ratner has reasonably and rationally inferred from the existing evidence that Coach Allen's exposure to Toluene was sufficient to support her opinion that it acted as a neurotoxin to accelerate/hasten the ALS course. As she explains in her report (**Tab 2**, pages 29-30), the Occupational Safety and Health Administration (OSHA) has created "permissible" levels (PELs) by which a worker can safely be exposed to Toluene; levels greater than the PEL therefore expose the worker to potential neurotoxic effects. Toluene's known neurotoxic effects include the exact symptoms suffered by Coach Allen as well as his staff: dizziness, nausea and headaches. Based on these reported symptoms and the results of the findings reported in the studies cited by OSHA, Coach Allen necessarily was exposed to concentrations that at least exceeded the OSHA PEL, established to protect workers against the health effects of exposure to hazardous substances.

4. **Dr. Oliver's Opinion**

Dr. Oliver concludes, consistent with Dr. Ratner, that Coach Allen had ALS and died as a result of his disease. [7] Mr. Allen was diagnosed with ALS by his treating physicians in January/February, 2002. His medical records and death certificate indicate that he died less than two years later as a consequence of his disease. Dr. Oliver concludes that Coach Allen had sporadic ALS. There is no evidence of a family history of ALS.

[7] Dr. Oliver also provides an opinion as to the defendants' liability, in failing to warn Coach Allen or otherwise use due care in protecting him from exposure to the solvents used in their re-surfacing work, but that opinion is not subject to this *Daubert* inquiry.

Dr. Oliver also concludes that the time of onset and rate of progression of ALS in Mr. Allen's case were causally related to his exposure to solvent vapors and aerosols during the course of the installation of the defendants' flooring system in the Field House of The College of the Holy Cross. The symptoms which Mr. Allen and his colleagues developed during this time period are consistent with neurotoxic effects of solvents – namely headache, dizziness, nausea, and disorientation. Dr. Oliver concurs with Dr. Ratner: the occurrence of these symptoms and their persistence suggest that exposures were at or above the permissible exposure limit (PEL) established by OSHA. The nature of Coach Allen's symptoms and the distinct temporal relationship between their onset and persistence and the installation of the flooring system are consistent with and make likely a causal association.

As Dr. Oliver explains in her report, the cornerstones to the determination of exposure-related disease in occupational medicine are: consistency of symptoms and clinical manifestations with what would be expected to occur in association with a given exposure and a temporal association between onset/worsening of symptoms and that exposure; and the use of differential diagnosis to exclude other possible causes. The application of the differential diagnostic method to the review of Mr. Allen's medical records, Mrs. Allen's deposition testimony, and the affidavits of co-workers who knew Mr. Allen well, reveals that he was active and healthy prior to the exposures incurred in the early summer of 2001. There is no family history of ALS; so that he did not have familial ALS. Other causes include exposure to pesticides and "agricultural chemicals" (which contain solvents), sixty hertz magnetic fields, and welding fume. There is no evidence that Mr. Allen materially was exposed to these agents.

Dr. Oliver herself reviewed Dr. Ratner's report and concludes that Ratner has provided ample evidence of the motor neuron toxicity of solvents generally, and Toluene specifically, with an emphasis on enzymatic and biochemical mechanisms. Dr. Oliver also conducted an independent review of in-vitro data from toxicological studies, in-vivo data from animal studies, and epidemiologic data from studies in human populations in a number of different countries, all of which supports a causal association between solvent exposure and the exacerbation of sporadic ALS.

5. Mr. Ewing's Opinion

William Ewing is the Technical Director for Compass Environmental, Inc. located in Georgia. Mr. Ewing is certified in the comprehensive practice of industrial hygiene by the American Board of Industrial Hygiene. He also passed the sub-specialty examination in Indoor Environmental Quality.

For 29 years, most of his work has focused on the identification, evaluation and control of airborne contaminants. This includes anticipating the release of contaminants during various work activities, determining pathways of exposure, measuring exposures to workers and bystanders, and controlling exposures following the hierarchy of controls concept. As an industrial hygienist he is knowledgeable of general and local exhaust ventilation principles, design and operation. He is familiar with the regulations affecting workers' exposures to chemicals promulgated by the Occupational Safety and Health Administration (OSHA), recommended practices and guidelines put forth by the National Institute for Occupational Safety and Health (NIOSH), the ACGIH, and other organizations.

Mr. Ewing's detailed report (**Tab 6**) explains the process by which the Holy Cross gym floor was re-surfaced and how the materials used, in particular Toluene, provided sufficient exposure levels to cause a neurotoxic reaction. It is Mr. Ewing's opinion to a reasonable degree of scientific certainty that Coach Dan Allen and some of his co-workers present in the field house during the gymnasium floor resurfacing were exposed to significant concentrations of solvent vapors during at least three days of the work. Based on the information reviewed to date, it is likely since industrial hygienists must consider groups of chemicals having the same target organs together as a mixture, that Mr. Allen's exposure to this mixture of solvents known to act on the central nervous system approached or exceeded neurotoxic levels.

Defendants offer no expert in rebuttal to Mr. Ewing.

6. Legal Argument

The admission of expert testimony is governed by Rule 702 of the Federal Rules of Evidence, which provides that:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

In applying Rule 702, the U. S. Supreme Court in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993) held that, in order to be admissible, scientific expert testimony must be both *relevant* and *reliable*. To determine whether scientific evidence is reliable, the Court enumerated four tests, or factors: (1) whether the scientific theory or technique can be (and has been) tested; (2) whether the theory or technique has been

subjected to peer review and publication; (3) whether a particular technique has a known potential rate of error; and (4) whether the theory or technique is generally accepted in the relevant scientific community. *Id.* at 593-594.

Ordinarily, whether a theory or technique can be (and has been) tested will be a major factor in determining its admissibility. *Id.* at 593. Peer review and publication are also commonly relied-upon elements. *Id.* However, the factors that the Court enumerated do not function as a definitive checklist, and no single factor will dispose of the reliability inquiry. *See Id.* at 592-95; *Anello v. Shaw* Indus., No. 95-30234-FHF, 2000 U.S. Dist. LEXIS 6835, at *12 (D. Mass. Mar. 31, 2000) (holding lack of studies supporting plaintiff's expert's conclusions not sufficient to prevent admission of testimony);[8] *Kennedy v. Collagen Corp.*, 161 F.3d 1226, 1229 (9th Cir. 1998) (finding district court abused its discretion by excluding expert testimony that was based on reliable methodology simply because "no epidemiological or animal studies" linked defendant's product to plaintiff's disease). Publication does not always correlate with reliability. *Daubert*, 509 U.S. at 593. Some ideas may be too new or of insufficient interest to have warranted publication, *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 151 (1999), and neither publication nor peer review is a *sine qua non* of admissibility. *Daubert*, 509 U.S. at 593.

In some cases, the *Daubert* factors may have no bearing at all, *see United States v. Hankey*, 203 F.3d 1160, 1169 (9th Cir. 2000); *United States v. Frazier*, 322 F.3d 1262, 1266-1267 (11th Cir. 2003), and the court may fashion new criteria that are relevant to

[8] " The very essence of expert testimony and any "battle of the experts" arises from the inherent uncertainty in these types of cases…This uncertainty leads to the very need for the jury to determine the facts from the differing and often completely opposite opinions held by equally qualified experts from the same field testifying in a single case." *Id.*

the specifics to that case. *Smith v. General Electric Co.*, No. 91-12912-RGS, 2004 U.S. Dist. LEXIS 7011, at *10 n.10 (D. Mass. Apr. 23, 2004). A number of courts have admitted medical testimony that relies heavily on a temporal relationship between an illness and a causal event. *See, e.g., Zuchowicz v. United States*, 140 F.3d 381, 385 (2d Cir. 1998); *Kannankeril v. Terminix Int'l, Inc.*, 128 F.3d 802, 809 (3d Cir. 1997). The temporal relationship will often be (only) one factor, and "how much weight it provides for the overall determination of whether an expert has 'good grounds' for his or her conclusion will differ depending on the strength of that relationship." *Heller v. Shaw Indus.*, 167 F.3d 146, 154 (3rd Cir. 1999).

The *Daubert* Court also imposed a special relevancy requirement. *See Daubert*, 509 U.S. at 591-92. "To be admissible, expert testimony must be relevant not only in the sense that all evidence must be relevant, *see* Fed. R. Evid. 402, but also in the incremental sense that the expert's proposed opinion, if admitted, likely would assist the trier of fact to understand or determine a fact in issue." *Ruiz-Troche v. Pepsi Cola Co.*, 161 F.3d 77, 81 (1st Cir. 1998); *See Daubert*, 509 U.S. at 591-92. In other words, Rule 702 "requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility." *Id.* at 592.

Regardless of the criteria used to determine reliability, the burden on the party seeking admission of the testimony is not to establish the scientific certainty of the proposed testimony, but to show, by a preponderance of the evidence, that the testimony is based upon valid scientific principals and methodology. *Daubert*, 509 U.S. at 593 n.10; *United States v. Monteiro*, 407 F.Supp. 2d 351, 372 (D. Mass. 2006). Nor does *Daubert* require or allow the trial courts to determine which scientific position is most likely

correct, the proponent of the evidence need only show that it was achieved in a scientifically sound and reliable manner. *Ruiz-Troche* 161 F.3d at 85; *see Smith,* 2004 U.S. Dist. LEXIS 7011, at *15 (holding court could not exclude plaintiff's expert testimony, despite belief that scientific opinion and epidemiological studies favored the defendant).

Daubert and its progeny represent a relaxing of the "general acceptance" test of *Frye v. United States*, 54 App. D.C. 46, 293 F. 1013 (D.C. Cir. 1923); *Smith*, 2004 U.S. Dist. LEXIS 7011, at *8; *United States v. Green*, 405 F. Supp. 2d 104, 118 (D. Mass. 2005). This is particularly true for new theories which may be too recent to have achieved acceptance in the scientific community. *United States v. Hines*, 55 F. Supp. 2d 62, 66 (D. Mass. 1999). The U.S. Supreme Court has expressed a preference for admitting evidence that may be borderline. "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." *Daubert*, 509 U.S. at 596; *Ruiz-Troche*, 161 F.3d at 85; *Smith*, 2004 U.S. Dist. LEXIS 7011, at *15. [9]

"As long as an expert's scientific testimony rests upon "good grounds, based on what is known," *Daubert*, 509 U.S. at 590 (internal quotation marks omitted), it should be tested by the adversary process - competing expert testimony and active cross-examination - rather than excluded from jurors' scrutiny for fear that they will not grasp its complexities or satisfactorily weigh its inadequacies. *See id.* at 596. In short, *Daubert* neither requires nor empowers trial courts to determine

[9] The traditional safeguards of directing a verdict and summary judgment are the "appropriate safeguards" for insufficient scientific testimony, rather than its "wholesale exclusion" under the general acceptance standard. *Daubert*
509 U.S. at 596, *G.E. v. Joiner, 522 U.S. 136, 155 (1997).*

which of several competing scientific theories has the best provenance. *Ruiz-Troche*, 161 F.3d at 85; *See Smith*, 2004 U.S. Dist. LEXIS 7011, at *15-*16. It demands only that the proponent of the evidence show that the expert's conclusion has been arrived at in a scientifically sound and methodologically reliable fashion. *Ruiz-Troche*, 161 F.3d at 85.

The First Circuit has held "[t]he ultimate purpose of the Daubert inquiry is to determine whether the testimony of the expert would be helpful to the jury in resolving a fact in issue." *Hochen v. Bobst Group, Inc.*, 290 F.3d 446, 452 (1st Cir. 2002) (quoting *Cipollone v. Yale Indus. Prods.*, 202 F.3d 376, 380 (1st Cir. 2000)). In making this determination, the Court must consider, "given the proffered expert's background, whether the scientific, technical, or other specialized knowledge he offers will assist the trier better to understand a fact in issue." *Gaydar v. Sociedad Instituto Gineco-Quirurgico y Planificacion Familiar*, 345 F.3d 15, 24 (1st Cir. 2003) (internal quotation omitted). Moreover, the court enjoys "substantial discretion" in deciding whether to admit or exclude relevant expert testimony. *Mitchell v. United States*, 141 F.3d 8, 15 (1st Cir. 1998) (citing *General Electric Co. v. Joiner*, 522 U.S. 136 (1997)).

"The inquiry envisioned by Rule 702 is a flexible one. Its overarching subject is the scientific validity -- and thus the evidentiary relevance and reliability -- of the principles that underlie a proposed submission." *Daubert*, 509 U.S. at 594-95.

Conclusion

For all the reasons set forth here, supported by the attached Rule 26 reports, Plaintiffs meet the FRE 702 and *Daubert* tests. The Court should permit the jury to hear their opinions at trial.

Respectfully Submitted,
The Plaintiff
By her Attorneys

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Dated: November 1, 2007

Certificate of Service

I hereby certify that a copy of the foregoing was served this day via ECF to the following counsel:

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Education and Degrees

Undergraduate

1995	Boston University College of Liberal Arts Bachelor of Arts in Psychology

Graduate

May 2004	Doctor of Philosophy Behavioral Neurosciences Program Boston University School of Medicine

Post-Doctoral Training

2004-2007	Post-Doctoral Fellowship Laboratory of Molecular Neurobiology Department of Pharmacology and Experimental Therapeutics Boston University School of Medicine (Mentor: David H. Farb, PhD)

ACADEMIC APPOINTMENTS

1998-present	Research Associate Department of Neurology Boston University School of Medicine
2004-present	Research Associate Department of Pharmacology and Experimental Therapeutics Boston University School of Medicine

PROFESSIONAL EXPERIENCE

Teaching

2000	Seminar Lecturer Integrated Clinical Problems Topic: *n*-Hexane Neurotoxicity Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine (Course Coordinator: Allen Geller, Ph.D)
2000-	Instructor Course Title: Toxicology Program in Biomedical Laboratory and Clinical Sciences Department of Biochemistry Boston University School of Medicine and Metropolitan College (Program Director: Connie Phillips, MA, MPH)
2001-	Instructor Course Title: Forensic Toxicology Program in Biomedical Laboratory and Clinical Sciences Department of Biochemistry Boston University School of Medicine and Metropolitan College (Program Director: Connie Phillips, MA, MPH)
2002	Guest Lecturer in Neurotoxicology Course Title: Introductory Toxicology Department of Environmental Health Boston University School of Public Health (Course Director: Wendy Heiger-Bernays, PhD)
2003-	Lecturer in Forensic Neurotoxicology Course Title: Forensic Neuropsychology Behavioral Neurosciences Program Boston University School of Medicine (Course Directors: Paul Spiers, PhD)
2004	Guest Lecturer in Neurotoxicology Course Title: Neuroscience Biology of Disease Course Boston University School of Medicine (Course Director: Thomas Brown, MD)

2004-	Robert G. Feldman Memorial Lecturer in Occupational Neurological Disorders and Neurotoxicology Course Title: Introduction to Occupational and Environmental Medicine Occupational Health Program Department of Environmental Health Harvard School of Public Health (Course Director: David Christiani, MD)
2005	Invited CME Lecturer Massachusetts Neuropsychological Society Title of Presentation: "Exciting New Frontiers in Neuropsychology: Magnetic Resonance Spectroscopy: The Case for Lead Exposure". Spaulding Rehabilitation Hospital, Boston, MA, February 1st, 2005.

Research

1995-1996	Research Assistant Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine (Program Director: Robert G. Feldman, M.D.)
1996-1998	Editorial Research Assistant Publication: "*Occupational and Environmental Neurotoxicology*" Author: Robert G. Feldman, M.D. Publisher: Lippincott-Raven, 1999 Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine
1998-2004	Senior Toxicologist and Project Manager Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine (Principal Investigator: Robert G. Feldman, M.D.)
2002-2004	Project Manager Gene-Metal Interactions and Parkinson's Disease Sponsor NIEHS Principal Investigators: Howard Hu, MD, ScD, MPH and Robert G. Feldman, MD

2004-	Research Associate and Project Manager Laboratory of Molecular Neurobiology Department of Pharmacology and Experimental Therapeutics Boston University School of Medicine (Chairman and Principal Investigator: David H. Farb, PhD)

Clinical

1998-	Senior Toxicologist Environmental and Occupational Neurology Program Department of Neurology Boston University School of Medicine Boston, MA

Business

2002-2004	Vice President and CEO Chemical Safety Net. Inc. Boston, MA and Delaware, MD

PROFESSIONAL AWARDS AND HONORS

2000-	Who's Who of American Women
2002-	Who's Who in America
2002-	Who's Who in Science and Engineering

PROFESSIONAL ORGANIZATIONS

1998-	Massachusetts Neuropsychological Society
1999-	American Academy of Clinical Toxicology
1999-	International Neurotoxicology Association
1999-	Society for Neuroscience
2000-2004	Society for Occupational and Environmental Health
2001-	American Conference of Governmental Industrial Hygienists
2001-	New York Academy of Sciences

PRESENTATIONS

1. **Ratner M,** Cabello, D, Thaler D, and Feldman R: Movement Disorder in an Adult Following Exposure to DEET. Presented at the North American Congress of Clinical Toxicology, Montreal, Quebec, Canada, October 6, 2001.
2. **Ratner MH,** Desbien S, Pierce RC, Gibbs TT, and Farb DH: Pregnanolone hemisuccinate inhibits reinstatement of cocaine seeking behavior in rats. Presented at the Society for Neuroscience Annual Meeting, Georgia World Congress Center, Atlanta, GA, October 17, 2006.

PUBLICATIONS

1. Feldman RG, **Ratner MH,** and Ptak T: Chronic toxic encephalopathy in a painter exposed to mixed solvents. Harvard School of Public Health, Grand Rounds in Environmental Medicine. Environ Health Perspect, 107(5): 417-422, 1999.
2. Feldman RG, **Ratner MH**, and Feldman ES: Approach to neurotoxicity tort cases. Neurologic Clinics: Medical-Legal Issues Facing Neurologists. Vol 17 (2):267-281, 1999.
3. Feldman RG, and **Ratner MH**: The pathogenesis of neurodegenerative disease: neurotoxic mechanisms of action and genetics. Current Opinion in Neurology, 12:725-731, 1999.
4. Feldman RG, and **Ratner MH**: Essentials of Metal Neurotoxicity: Mechanisms and Pathology. Clinics in Occupational and Environmental Medicine: Neurotoxicology. 1(3):1526-1546, 2001.
5. **Ratner MH**, Feldman RG, and White RF: Neurobehavioral Toxicology. In: Ramachandran V.S. (Ed); Encyclopedia of the Human Brain. New York, Elsevier Science, Vol. 3, pp 423-439, 2002.
6. Feldman RG, and **Ratner MH**: Behavioral Syndromes in Neurotoxicology. In: Fogel BS, Schiffer RB, and Rao SM (eds): Neuropsychiatry. 2nd Edition. Philadelphia, Lippincott-Williams and Wilkins, pp1168-1190, 2003.
7. Feldman RG, and **Ratner MH**: Treatment of Neurotoxic Effects of Gases: Carbon Monoxide, Hydrogen Sulfide, and the Nitrogen Oxides. In: Noseworthy, J. (ed); Neurological Therapeutics: Principles and Practices. London, Martin Dunitz, pp 1526-1530, 2003.
8. Feldman RG, and **Ratner MH**: Heavy Metal Poisoning. In: Lynn, D. J., Newton, H.B., and Rae-Grant, A.D. (eds): The 5-Minute Neurology Consult. Philadelphia, Lippincott, Williams & Wilkins, pp 218-219, 2004.
9. **Ratner MH**, and Feldman, RG: Environmental Toxins and Parkinson's Disease. In: Pfeiffer, R.F., and Ebadi M. (eds): Parkinson's Disease. Boca Raton, CRC Press, Chapter 6, pp 51-62, 2005.
10. Feldman RG, Janulewicz PA, and **Ratner MH**: Toxic encephalopathy. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 189-194, 2005.
11. Feldman RG, and **Ratner MH**: Peripheral neuropathy. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 388-394, 2005
12. Feldman RG, and **Ratner MH**: Tremor. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 488-491, 2005.
13. Feldman RG, Janulewicz PA, and **Ratner MH**: Memory impairment. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing

Occupational Disease and Injury. American Public Health Association Publication, pp 332-335, 2005.

14. Feldman RG, Janulewicz PA, and **Ratner MH**: Parkinsonism. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 376-382, 2005.
15. Feldman RG, Nelson S, and **Ratner MH**: Multiple Sclerosis. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 361-365, 2005.
16. Feldman RG, Nelson S, and **Ratner MH**: Smell and Taste Disorders. In: Levy BS, Wagner GR, Rest KM, and Weeks JL (eds.); Preventing Occupational Disease and Injury. American Public Health Association Publication, pp 454-457, 2005.
17. **Ratner MH** and Jabre J: Treatment of Neurotoxic Effects of Gases: Carbon Monoxide, Hydrogen Sulfide, and the Nitrogen Oxides. In: Noseworthy, J.H. (ed); Neurological Therapeutics: Principles and Practices. Chapter 148, London, Martin Dunitz, pp. 1701-1706.
18. **Ratner MH** and Jabre J: Treatment of Neurotoxic Effects of Organic Solvents. In: Noseworthy, J.H. (ed); Neurological Therapeutics: Principles and Practices. Chapter 147, London, Martin Dunitz, pp1694-1700.

Abstracts

1. **Ratner M,** Cabello, D, Thaler D, and Feldman R: Movement disorder in an adult following exposure to DEET. J Toxicol Clin Toxicol, 39: 477, 2001.
2. **Ratner MH,** Desbien S, Pierce RC, Gibbs TT, and Farb DH: Pregnanolone hemisuccinate inhibits reinstatement of cocaine seeking behavior in rats. Society for Neuroscience, 591.13/PP79, 2006.
3. **Ratner MH,** Desbien S, Kostakis E, Pierce RC, Gibbs TT, and Farb DH: Pregnanolone hemisuccinate inhibits reinstatement of cocaine seeking behavior in rats. New England Pharmacologists Annual Meeting, 2007.
4. **Ratner MH,** Desbien S, Kostakis E, Pierce RC, Gibbs TT, and Farb DH: Pregnanolone hemisuccinate inhibits reinstatement of cocaine seeking behavior in rats. American Society of Pharmacology and Experimental Therapeutics Annual Meeting, 2007.

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	)	CIVIL ACTION NO. 05-40048-FDS

RULE 26 EXPERT REPORT – DR. MARCIA RATNER

Introduction

I have been asked to examine the role of Mr. Dan Allen's subacute (repeated exposures occurring over a relatively short period of time; typically defined as a duration of 1 month or less) exposure to neurotoxic chemicals in May/June 2001 (during the course of a gym floor re-surfacing in the building where Mr. Allen worked) and the subsequent onset of his amyotrophic lateral sclerosis (ALS) condition (also known as Lou Gehrig's disease), which resulted in Mr. Allen's death on May 16, 2004.

I have concluded to a reasonable degree of scientific certainty, that: (a) the neurotoxic chemicals to which Mr. Allen was exposed are capable of altering and hastening the course of neurodegenerative diseases such as ALS; and (b) Mr. Allen's exposure to these chemicals was at least a substantial contributing factor in hastening the early onset of his ALS such that he would not likely have died from his ALS disease until later in life.

This report begins with an overview of my opinion that the neurotoxic chemicals to which Mr. Allen was exposed are capable of altering and hastening the course of neurodegenerative diseases such as ALS. The details which support this overview are addressed later in this report.

A. Overview of My "General" Causation Opinions

Most of this report delves into a good amount of scientific, pharmacological, and toxicological terminology and principles, which can be confusing or complicated for lay readers, but I have endeavored to explain my scientific bases as accurately and completely as possible. I therefore offer in this section, a more digestible summary of the underlying basis for my General Causation opinion, that the chemicals to which Dan Allen was exposed (and mostly I examine the chemical Toluene) were capable of hastening the onset of his ALS. It is really quite logical:

1. While science does not know what causes ALS, science does understand, and it is generally accepted as to how ALS occurs; that is, we do understand the neuropathology and the mechanisms by which neurodegeneration occurs, and I have described these mechanisms below.

2. The chemicals to which Dan Allen was exposed, and in particular Toluene, are known and generally accepted neurotoxicants; that is, they are toxic to, and can kill, human neurons.

3. Science also knows the mechanisms by which Toluene acts as a neurotoxicant, and this knowledge is also generally accepted; I have described these mechanisms below.

4. The mechanisms by which neurodegeneration occurs in ALS are exactly the same mechanisms by which Toluene acts upon neurons.

5. Scientific logic therefore dictates that Toluene is capable of altering or hastening subclinical and clinical course of ALS since the interaction of the toxic effects of toluene with the neuropathological mechanisms implicated in ALS will result in an additive effect.

6. We know that Dan Allen was exposed to sufficient levels of Toluene to succumb to its neurotoxic effects, because we know he presented with neurologic symptoms (headaches, dizziness) in exquisite temporal association with his exposure. I will demonstrate later in this document that the levels of exposure associated with the symptoms Dan Allen experienced were in excess of the current federal government Permissible Exposure Limit (PEL) of 200 parts per million (ppm) (see 29 CFR 1910.1000). We do not need to know a more specific level of exposure in order to make the causal inference here.

7. While few studies have looked at age at onset of ALS among subjects exposed to chemicals, many researchers have looked for chemicals that can slow the disease. The NINDS (National Institute of Neurological Disorders and Stroke) recognizes that the clinical course of the disease can be slowed by certain chemicals. "No cure has yet been found for ALS. However, the FDA has approved the first drug

treatment for the disease *riluzole*. Riluzole is believed to reduce damage to motor neurons and prolongs survival by several months, mainly in those with difficulty swallowing". [NINDS ALS information webpage; Miller RG *et al* 2005] *Riluzole, is a putative glutamate release blocker* that has modest benefit in extending survival, and is the only medication approved by the FDA for the treatment of ALS. [PDR, 2005, pp 744-746].

8. If a chemical can be used as a pharmaceutical to extend survival in ALS, can exposure to a chemical also curtail survival (or in order words, hasten onset of ALS)? To answer this question we will identify below putative points of interaction between the chemicals to which Mr. Allen was exposed in his workplace and the mechanisms of neurodegeneration implicated in ALS.

9. For example, if oxidative stress is implicated in ALS and Mr. Allen was exposed to a chemical that increases oxidative stress, then we have identified a putative point of interaction. Likewise, if increased glutamatergic neurotransmission is implicated in ALS and Mr. Allen was exposed to a chemical that increases glutamatergic neurotransmission, then we have identified another putative point of interaction.

10. In fact, review of the literature on ALS and the Material Safety Data Sheets of the chemicals used by Martin Surfacing to perform the floor re-surfacing at issue, clearly demonstrates that these were two of the ways in which the exposures that occurred during the floor refinishing process interacted with the latent disease from which Mr. Allen eventually died.

11. I will therefore present herein peer-reviewed scientific data supporting the conclusion that Mr. Allen's exposure to Toluene and other compounds used in the floor refinishing process at Holy Cross unmasked his latent ALS and was at least a substantial contributing factor to the progression of his disease.

My qualifications, the generally accepted method I followed in reaching this conclusion, and all the scientific bases upon which I rely in making these opinions, now follow.

B. My Qualifications

1. My professional education, experience and training have created a unique combination of clinical, academic and laboratory-based expertise in the very subject matter at issue in this legal case: assessing the causal role of an exposure to neurotoxic chemicals to the onset of a neurodegenerative disease. There are few scientists in the country with this clinical/academic/bench-science background. A copy of my CV is appended; and summarized as follows:

2. In 2004, I earned my Ph.D. from Boston University School of Medicine's Behavioral Neurosciences Program. I trained and worked directly with Robert

Feldman, M.D., generally considered one of, if not the world's foremost experts in neurotoxicology. From 1998-2004, I was the Senior Toxicologist and Project Manager working in conjunction with Dr. Feldman under the Department of Neurology's Environmental and Occupational Neurology Program. Our work resulted in several articles, textbook chapters and other professional writings, most of which are peer-reviewed, on the subject of neurotoxicology and neurodegenerative disorders. I am the co-author of those writings. Today, I remain the Senior Toxicologist for the Environmental and Occupational Neurology Program at the Boston University School of Medicine.

3. Between 2004 and 2007, I conducted and completed a post-doctoral fellowship supported by an NIH training grant in Aging in the Laboratory of Molecular Neurobiology within the Department of Pharmacology and Experimental Therapeutics at the Boston University School of Medicine. I focus my work in the lab in assessing the *in vivo* effects of novel chemicals, which may be developed into new drugs to address neurological and psychiatric disorders including neurodegenerative diseases. In that capacity, I have become an expert in the toxicological and pharmacological methods used by academic and industrial researchers to assess the ability of chemicals to alter the course of neurological disease.

4. Since 2004, I have been a research associate in the Department of Pharmacology and Experimental Therapeutics. In that regard, I am well studied and experienced in: (a) the scientific method for research; (b) biostatistics and epidemiology; the ability to understand and apply the results of scientific studies to consideration of causal assessment; and (c) assessing the quality of scientific studies.

5. Since 1998, I have been a research associate in the Department of Neurology at the Boston University School of Medicine. In that role, I have worked as a clinical research scientist evaluating patients with neurological conditions, including neurodegenerative disease such as ALS. I have worked closely with Dr. Joseph Jabre, the former chair of neurology at the VA Hospital and a faculty member at the School of Medicine at Boston University. As a research associate, I have become well-versed and experienced in the diagnosis and treatment of patients with neurodegenerative disorders. I am fully competent in performing clinical evaluations of such patients.

6. In recognition of my cross-over background in clinical neurology, pharmacology and expertise in neurotoxicology, I have been invited to lecture classes at the Boston University School of Medicine's Departments of Neurology, Biochemistry, Environmental Health, Behavioral Neuroscience Program; in addition, I have been an invited lecturer at the Harvard School of Public Health and the Massachusetts Neuropsychological Society. I have lectured to these classes in the following topics: Neurological Disorders and Neurotoxicology, Forensic Neuropsychology, Introductory Toxicology, Forensic Toxicology, and Neurotoxicity.

C. Overview of General Causal Inference in Science

1. This report presents my expert opinions on the role of Dan Allen's exposure to neurotoxic chemicals in May/June 2001 to the onset of, and death from ALS. So in effect, I examine two "big picture" questions: (a) whether the neurotoxic chemicals to which Mr. Allen was exposed are capable of altering or hastening the course of a neurodegenerative disease like ALS (we can refer to this as "General Causation"); and (b) whether this exposure was at least a substantial contributing cause to hastening the course of Mr. Allen's ALS (we can refer to this as "Specific Causation"). Before discussing my opinions, it may be valuable to briefly discuss the principles of General causal inference in science.

2. General Causation in science is an inference, a judgment based upon observational and experimental deductions as well as an understanding of the general laws of nature.

3. It is simply common sense that a single study is generally not sufficient for a causal inference. That is why the conclusions of most studies, no matter how large or small, speak in terms of their results "suggesting" that, for example, A is implicated in B. Published and peer-reviewed scientific studies almost never speak in language of "causation". So, as will be seen in this report, many studies are cited which make "suggestions" based upon well-designed and carried out methods. These studies, along with other methods of the scientific process, then form the basis for making a causal inference. Another way of thinking of the use of the word "suggests" when it appears in scientific literature is, "provides evidence in support of".

4. So, as a scientist, I am obligated to consider all available scientific evidence in assessing a causal inference. That includes large epidemiologic case-control studies, but also the smallest experimental studies looking at a handful of rats (or even just looking at molecules), or anecdotal reports of events occurring in a few persons, as well as the pharmacology, toxicology, biologically plausible theories and mechanisms of actions. The fact that a study has flaws or is not "statistically significant" does not mean the study should be disregarded; indeed, it is scientifically inappropriate to fail to consider the cumulative effect of all scientific evidence.

5. In the real world, scientists and physicians infer causation from the totality of several lines of evidence that, together, comprise the body of existing scientific data. That is precisely what I have done here.

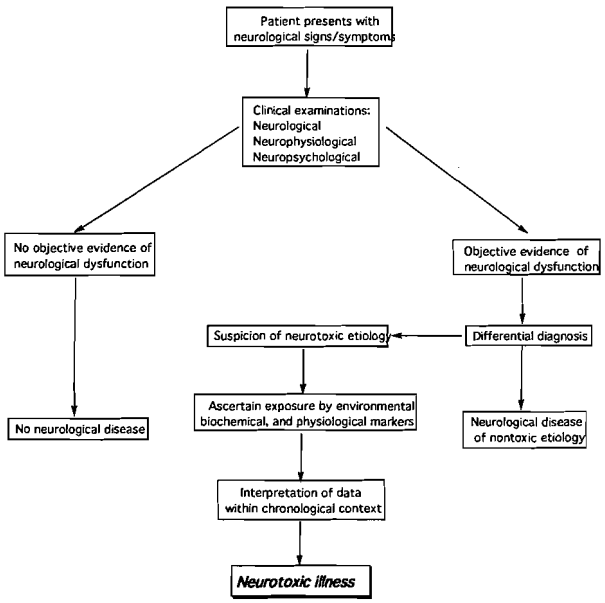
D. The Generally Accepted Scientific Method for Assessing Causation in Neurotoxicity Legal Cases

1. Just as there is an accepted method in assessing General Causation, so too there is a generally accepted method in neurotoxicity cases to assess Specific Causation.

2. It so happens that Dr. Feldman and I developed the diagnostic algorithm for this assessment. In our textbook, Occupational and Environmental Neurotoxicology (Lippincott-Raven 1999), we proposed a method for assessing specific causation in cases like that of Dan Allen. Our method has been received by scientific community and has been published in peer-reviewed journals without criticism. For example, we presented our model in the well-respected and peer-reviewed professional series, Neurologic Clinics in May 1999, in an article entitled, "Approach to Neurotoxicity Tort Cases". This article was invited by the editor of this series in recognition of our expertise in the area.

3. As it has now withstood the test of time for more than seven years, it can be considered generally accepted.

4. This can be diagrammed as follows:



5. I have followed this generally accepted method for assessing Specific Causation in the case of Dan Allen, as discussed below.

E. My Factual Assumptions

I have been asked to assume the following facts as relate to my consideration of this case:

1. In May/June 2001, Dan Allen was the head coach of the football program at the College of the Holy Cross. He was 45 years old and in good physical health. There was no history of ALS in his family.

2. In late May through early June, 2001, employees of Martin Surfacing re-surfaced the gym floor in the building known as the Field House at the college. Mr. Allen's office was located on the second floor of the Field House.

3. Mr. Allen was present throughout the course of the re-surfacing work.

4. The workers performing the re-surfacing made use of several chemicals, all as listed on certain MSDS sheets provided to me. These chemicals included toluene, xylene, methyl isobutyl ketone, ethyl benzene, titanium dioxide, propyleneglycol methylether acetate, dipropyleneglycol methylether acetate, isophorone diisocyante, methylenebis cyclohexylisocyanate, and Stoddard solvent (Stoddard solvent is a petroleum distillate fraction containing C_7—C_{12} hydrocarbons, primarily straight-chain and branched-chain alkanes and cycloalkanes; it may also contain up to 20% aromatic hydrocarbons.).

5. During the re-surfacing work, Mr. Allen complained of and exhibited signs of neurological dysfunction, including headaches, dizziness and nausea. Other personnel from the college who worked and were present in the Field House during the re-surfacing work experienced similar problems.[1] It is important to note that the symptom of nausea is common response of the brain to excessive blood levels of a toxic chemical. This response occurs to facilitate expulsion of the offending toxic agent. Volunteers exposed to toluene developed slight nausea and lassitude at a concentration of 600 ppm (this is 3 times the OSHA PEL of 200 ppm and 100 ppm greater than the maximum peak concentration permissible by OSHA) [Clayton and Clayton in Patty's Industrial Hygiene and Toxicology, 1981-1982, p. 3283; Hathaway, Proctor, Hughes, and Fischman, Proctor and Hughes' chemical hazards of the workplace. 1991, p. 546].(http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html) (also see 29 CFR 1910.1000)

F. My Clinical Examination of Dan Allen

In addition to the above assumptions, along with Dr. Joseph Jabre, I had the important opportunity to meet Dan Allen, and conduct a clinical neurological examination of his condition prior to Mr. Allen's death. A summary of that examination follows:

1. Mr. Daniel Allen sought consultation with the Environmental and Occupational Neurology Program at the Boston University School of Medicine for possible toxic exposure related neurological symptoms on April 13, 2004. Mr. Allen is a 48 year-old left-handed gentleman with no significant past medical history. Prior to his early retirement due to his physical limitations related to his neurological manifestations, Coach Allen (as he is known by his peers) was the head football coach at Holy Cross.

[1] I have relied on the affidavits of one of the floor refinishers, and several co-workers of Coach Allen, as well as Mr. Allen's written journals and the deposition of Mrs. Allen. The affidavits are contained here; the other items I understand are in the possession of defense counsel.

2. Coach Allen's history revealed unwitting occupational exposure that occurred in May-June of 2001 when the gym floor at the college where he was employed was refinished. The refinishing process took at least one full workweek to complete. During the refurbishment process, Coach Allen worked in his office located adjacent to the gym, and experienced acute symptoms of dizziness, headaches, and disorientation. Other people in the area reportedly had similar acute symptoms. One month later, while he was on vacation, he experienced diarrhea, which improved spontaneously. Upon returning to work from his vacation he again experienced symptoms of headaches and dizziness similar to when he was first exposed although no refurbishment work was actively being performed on the gym floor at this time. Around this same time Coach Allen began to experience symptoms of fatigue and weakness for which he sought medical consultation with his primary care physician and a neurologist. He was started on Paxil at this time. He was seen by Dr. David Chad at the University of Massachusetts, Worcester and Dr. Russell at the Lahey clinic who did an EMG on him in February 2002. He also had CSF studies and a head MRI. In September 2001, he developed fasciculations in the lower extremities, which spread to the arms and now have decreased. He became wheelchair bound in the spring of 2003. He is currently wheelchair bound with contracture of hands and feet. He also has hypothyroidism.

3. On clinical neurological exam, Coach Allen spoke softly and ran out of breath easily but was nevertheless able to provide a good history with assistance from his wife and his friend, Kate. Cranial nerves II-XII were all normal except for tongue atrophy and fasics. DTRs were 2+ KJ, 0 AJ, 1-2+ BJ, 1+ BRJ. Toes? + Hoffman's. Strength exam revealed generalized weakness in both the upper and lower extremities. Hands and feet were curled and difficult to examine. Sensory exam shows, mild decrease to pinprick in lower extremities. Cerebellar exam could not be performed due to patient's motor limitations.

G. Clinical Overview of ALS

A general discussion about ALS will be helpful in understanding the opinions presented in this report.

1. The National Institute of Neurological Disorders and Stroke (NINDS) defines ALS as follows: Amyotrophic lateral sclerosis (ALS), sometimes called Lou Gehrig's disease, is a rapidly progressive, invariably fatal neurological disease that attacks the nerve cells *(neurons)* responsible for controlling voluntary muscles.

2. In ALS, both the upper motor neurons and the lower motor neurons degenerate or die, ceasing to send messages to muscles. Unable to function, the muscles gradually weaken, waste away, and twitch. Eventually the ability of the brain to start and control voluntary movement is lost.

3. Individuals with ALS lose their strength and the ability to move their arms, legs, and body. When muscles in the diaphragm and chest wall fail, individuals lose the ability to breathe without ventilatory support.

4. The disease does not affect a person's ability to see, smell, taste, hear, or recognize touch, and it does not usually impair a person's thinking or other cognitive abilities. However, several recent studies suggest that a small percentage of patients may experience problems with memory or decision-making, and there is growing evidence that some may even develop a form of dementia.

5. Approximately 20% of familial ALS cases are associated with mutations in SOD1, the gene encoding Cu/Zn-superoxide dismutase (CuZnSOD) (Rosen et al., 1993). The cause of sporadic ALS on the other hand is not known, and scientists do not yet know why sporadic ALS strikes some people and not others.

6. This last point is important for this expert report. I do NOT offer the opinion in this case that Dan Allen's chemical exposure caused his ALS. It is my opinion, to a reasonable degree of certainty, that Mr. Allen was genetically predisposed to develop ALS and would likely have seen the course of ALS progress fatally, later in life. It is my opinion to a reasonable degree of certainty that Mr. Allen's chemical exposure hastened an early onset of his ALS.

H. Review of Epidemiology Addressing Chemical Exposure and ALS

1. Epidemiology is generally and simply defined as the study of the patterns, causes and control of diseases in sample populations.

2. When relevant epidemiology is available, it can be a useful tool and must be considered in a scientist's General Causation assessment. Epidemiology is not useful to assess so-called Specific Causation.

3. Many epidemiological studies have focused on elucidating the etiology of ALS, and therefore have asked whether chemicals "cause" or "trigger" the disease. Although numerous solvents and other industrial chemicals have neurotoxic properties, past exposure to these agents is often difficult to quantify and validate making these studies difficult to design and interpret.

4. Nevertheless, Siddique and colleagues (see Saeed et al. 2006) recently concluded based on the findings of their most recent study that there is evidence of a significant association of variants in the paraoxonase gene with sporadic ALS and that this is compatible with the hypothesis that *environmental toxicity in a susceptible host may precipitate ALS*.

5. Several case-control studies have evaluated the risk of ALS among those reporting past occupational exposure to solvents. According to a report prepared

by Noonan et al., 2002 for the *Agency for Toxic Substances and Disease Registry* (ATSDR) the epidemiologic literature offers some support for an association between the risk for ALS and past exposure to organic solvents.

6. Unfortunately, most of these studies suffer from deficiencies with regard to exposure characterization and chemical specificity. A study in the United States reported a small but statistically significant elevated risk of ALS among those who self-reported solvent exposure. Although the investigators found no elevated risk when overall solvent exposure was assessed by an expert panel review of occupational histories, the expert panel assessment of occupational exposure to more specific groups of chemicals found elevated risk estimates for alcohols or ketones; benzene, ***toluene***, or ***xylene***; and cleaning solvents or degreasers (McGuire et al., 1997).

7. McGuire (1997) is the only study that evaluated the risk of ALS from exposure to individual, specifically identified, volatile organic compounds and it is interesting to note the two of the solvents to which Mr. Allen was exposed are among those associated with an increased risk.

8. While it is not the position of this document that any chemical causes ALS, the role of chemical exposures as modifying factors in the clinical course of the disease is demonstrable.

9. Although polymorphisms in enzymes involved in the metabolism of chemicals and age at onset of ALS has been studied, there are very few published reports that have looked specifically at the relationship between age at onset of ALS and antecedent events such as exposure history (Orru et al., 1999; Provinciali L, Giovagnoli, 1990; Saeed et al., 2006).

10. Among the possible reasons for the paucity of data is the simple fact that the answer is fairly intuitive as will be discussed further below (i.e., if exposure to neurotoxicants kills neurons and ALS kills neurons then the additive effects of the two events occurring in the same individual should be a younger age at onset of the disease).

11. The second reason is funding limitations; why spend money and time looking at factors that modify the clinical course of the disease when the more important question of what causes ALS has not yet been answered?

12. Moreover, and importantly, the only entities with the financial means to conduct epidemiological studies to examine the role of a specific chemical in altering the course of ALS, is the chemical industry, and while industry has the means to conduct such a study, it does not have the motivation to do so, for obvious business reasons. The reverse is true for the pharmaceutical industry, which invested millions of dollars on human clinical trials (the industry equivalent of

epidemiological studies) looking for chemicals that can slow the course of the disease, again for obvious business reasons.

13. Finally, a study that would examine the role of a specific chemical and its association with a disease like ALS, would be very expensive (on the order of millions of dollars) and take many years to complete.

14. Nevertheless, there has been a recent shift among those involved in neurodegenerative disease research in general toward elucidating the relationships between exposure history, genetics, and age at disease onset as the failure to identify a common genetic cause makes it increasing plausible that these types of disease involves multiple factors (Racette et al., 2001; Pezzoli et al., 2000; Wilk et al., 2006).

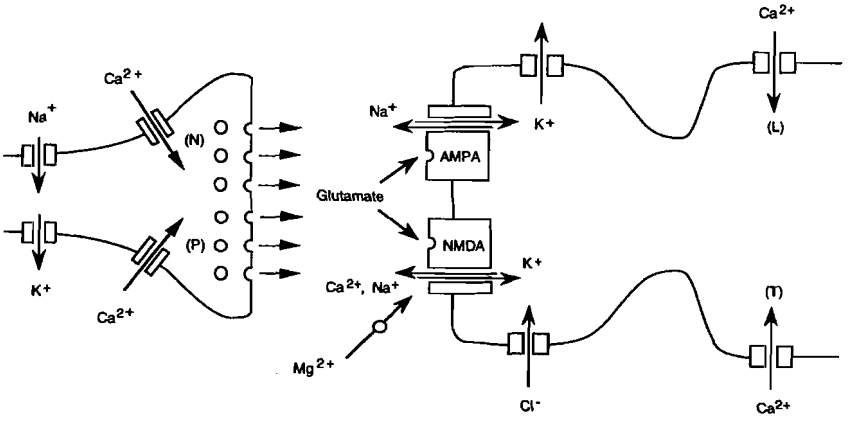
15. So, while there are no epidemiologic studies which contradict the position taken in this paper, there is admittedly little epidemiologic data which is directly on point. This is often the case when examining the neurotoxicity of chemicals, and yet scientists are constantly able to arrive at sound and rational causal inferences, through the scientific method, as I have done here.

I. Pathogenesis of ALS: Review of Generally Accepted Mechanisms of Action

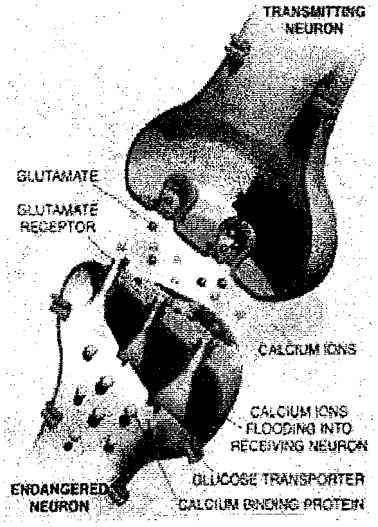
The following presents the generally accepted mechanisms by which neurodegeneration occurs in ALS (glutamatergic neurotransmission and oxidative stress).

I begin with some important concepts necessary to understand the neuroscience at issue, and then discuss the specific mechanisms at issue.

1. Communication between nerve cells is referred to as *neurotransmission*, which is mediated by *chemical messengers* known as neurotransmitters. Glutamate is an example of an excitatory neurotransmitter (i.e., a neurotransmitter that excites the next neuron in the chain of command). Upper motor neurons communicate with lower motor neurons by releasing glutamate. During glutamatergic neurotransmission (i.e., neurotransmission mediated by glutamate), glutamate released from the presynaptic or upstream neuron binds to and activates receptors located on the surface of the postsynaptic or downstream neuron. Activation of these excitatory glutamate receptors results in an influx of sodium (Na^+) and calcium (Ca^{2+}) ions into the cell body, which in turn causes the neuron to release its neurotransmitters (see Figure below). And so, the process continues until the final cell in the chain of command is activated (e.g. a muscle cell is signaled to contract).



2. *Excitotoxicity* is a type of neuronal degeneration mediated by over-stimulation of glutamate receptors. Experimental evidence indicates that glutamate mediated excitotoxicity contributes to neuronal damage in a number of neurodegenerative disorders including amyotrophic lateral sclerosis (ALS). The role of glutamate mediated excitotoxicity in ALS is related to the fact that upper motor neurons are glutamatergic (i.e., communicate with lower motor neurons by releasing glutamate). *Elevated extracellular glutamate* concentrations can occur when the release from presynaptic terminals is augmented or when re-uptake is insufficient. Adequate re-uptake is normally assured by glutamate transporters present in neurons and astrocytes. Elevated glutamate concentrations can also occur when glutamate is released from injured glutamatergic neurons. The release of glutamate into the extracellular space results in excitotoxic death of surrounding neurons (see figure below). This type of collateral damage is involved in the spread of the neurodegeneration following stroke and is associated with neurodegeneration in ALS (Van Den Bosch et al., 2007). As neurons die, the glutamate released is able to induce this excitotoxic cascade in more than one adjacent neuron. As more and more neurons die and more and more glutamate is released, the process begins to snowball and the progression of the disease increases. At a critical point, when the majority of the neurons have died, the disease essentially ceases to progress further.



3. Assuming that Mr. Allen's chemical exposure resulted in the death of even a single motor neuron, then the exposure contributed to the progression of his disease (It is my opinion that the exposure was at least a substantial contributing factor as expressed in this report). More importantly, the death of each glutamatergic motor neuron would result in the release of glutamate, which spills into the extracellular space where it reacts with receptors on adjacent neurons and can thereby induce something called "apoptosis" via excitotoxicity, thereby aggravating an already relentlessly progressive neurodegenerative process mediated by the increased glutamate released in association with the death of neurons due to ALS. This can effectively be thought of as being like a snowball rolling down a hill in that each dying neuron contributes to the death of other neurons. The only FDA approved pharmaceutical agent for treating ALS, riluzole, is administered in an attempt to slow this process.

4. *Apoptosis* is a form of programmed cell death in which the cell self-destructs when stimulated by the appropriate trigger. It is a genetically programmed event that can be triggered by a variety of internal or external stimuli. Apoptosis is characterized morphologically by cell shrinkage, membrane blebbing, chromatin condensation and fragmentation. These changes distinguish apoptosis from cell death by *necrosis,* which refers to the morphological changes associated with abrupt cell death as occurs following ischemia or physical trauma. In contrast to apoptosis, necrosis, is associated with disruption of cellular respiration and osmotic pressure, and with swelling that ultimately causes the cell to rupture.

5. *AMPA receptors are a type of glutamate receptor. AMPA mediated excitotoxicity is aggravated by chloride influx.* It has been shown in cultured rat spinal motor neurons that chloride influx aggravates Ca^{2+}-dependent AMPA receptor mediated motor neuron death. The membrane depolarization caused by AMPA receptor stimulation results in Cl^- influx through 5-nitro-2(3-phenylpropyl-amino) benzoic acid- and niflumic acid-sensitive Cl^- channels. This Cl^- influx aggravates excitotoxic motor neuron death by two mechanisms: (1) It increases the AMPA

receptor conductance; and (2) it also results in an elevation of the Ca^{2+} driving force through a partial repolarization. As a consequence, Cl^- ions can play a vital role in glutamate-mediated excitotoxicity (van Damme et al., 2003).

6. *Although Cl^- influx normally suppresses neuronal excitability and thereby counteracts the action of excitatory neurotransmitters such as glutamate, Cl^- influx during exposure to pathological amounts of glutamate can amplify the excitotoxic action of glutamate on motor neurons. Co-administration of GABA enhances the Cl^- influx during AMPA receptor stimulation and this results in an increased Ca^{2+} influx and enhanced cell death. These observations suggest that concomitant GABAergic stimulation may aggravate excitotoxic motor neuron death. This effect of Cl^- influx on excitotoxicity does not seem to be unique to motor neurons, as similar results were found in cerebellar granule cells.* (van Damme et al., 2003). I address Toluene in detail below, but it worth noting here that, like ethanol, Toluene reversibly enhances $GABA_A$ receptor-mediated synaptic currents in rat hippocampal slices (Beckstead et al., 2000). When GABA binds to the $GABA_A$ receptor the channel is opened and chloride ions enter the neuron (i.e., chloride influx is enhanced).

7. These findings provide evidence for just one of the mechanisms by which exposure to toluene can contribute to excitotoxic upper motor neuron death.

8. Unfortunately, it is much more likely that the chemical exposure Mr. Allen experienced resulted in the death of more than one motor neuron and that this process involved more than one mechanism of neurotoxicity. This neuronal loss would have been induced by direct neurotoxic effects as cited above and indirectly by the chemical exposure interfering with the ability of his body to scavenge "free radicals" and attenuate "oxidative stress" which importantly has been implicated in the progression of ALS (Chi et al., 2007; McDermott et al., 2007).

9. By definition a *free radical* is any atom (e.g. oxygen, nitrogen) with at least one unpaired electron in the outermost shell. Free radicals are highly reactive due to the presence of unpaired electron(s).

10. *Oxidative stress* is a commonly heard term that refers to the adverse effects that *reactive oxygen species (ROS) such as hydrogen peroxide and the free radicals super oxide and the hydroxyl radical have on the body.* Antioxidants such as vitamin E and vitamin C scavenge reactive oxygen species and prevent them from damaging tissues. Reactive oxygen species are chemicals that possess a lone electron. Electrons like to be paired with other electrons. When this does not happen quickly enough they will steal an electron from any nearby source. One such source is the lipid rich cell membranes of neurons. This reaction results in damage to the cell membrane referred to as lipid peroxidation, which is one type of neuronal cell damage that results from oxidative stress and is characterized by addition of a peroxide group to the cell membrane, which in turn alters the

membrane structure and its ability to function properly. Reactive oxygen species also damage mitochondrial membranes and thereby disrupt cellular respiration, which is critical to cell viability. ROS can also damage DNA and disrupt protein synthesis (Halliwell, 2006).

11. Approximately 20% of familial ALS cases are associated with mutations in SOD1, the gene encoding Cu/Zn-superoxide dismutase (CuZnSOD) (Rosen et al., 1993). Studies suggest that SOD1 mutation leads to cell death not only through a reduction in clearance of superoxide radical but through some other as yet undefined mechanism. Recently, mitochondrial-produced oxygen radicals have been found to play a critical role in mutant SOD1-mediated neuronal toxicity suggesting that mitochondrial-produced free radicals may be potential therapeutic targets in ALS (Zimmerman et al., 2007).

12. Studies suggest that free radicals both decrease depolarization-induced vesicular release and enhance basal, nonvesicular release of glutamate. In order to evaluate the contribution of oxidative reactions to this effect, the actions of the oxidizing agent chloramine-T on synaptosomal release of excitatory amino acids have been assessed. Basal and depolarization evoked [3H]D-aspartate release were found to be calcium-independent and nonvesicular. Chloramine-T pretreatment significantly increased basal release, while having no effect on high K(+)-evoked release. These data suggest that an oxidative process can mimic the free radical increase of basal release, as well as the decrease in synaptic potentials. On the other hand, calcium-independent-evoked release may involve a different mechanism. These results demonstrate that under basal, nondepolarizing conditions, oxidative stress exerts an adverse effect on the presynaptic nerve terminal, resulting in an increased release of potentially damaging excitatory amino acid neurotransmitters such as glutamate (Gilman et al., 1993).

13. Studies in mice expressing the mutant form of SOD1 indicate that supplementation with vitamin E can slow disease onset suggesting that an increase in oxidative stress is associated with disease onset and that this process can be attenuated by antioxidants (Gurney et al., 1996).

14. I will spend a moment also discussing something called "p75 neurotrophin receptor (p75NTR)". p75NTR is a member of the tumor necrosis factor receptor superfamily and acts as a death receptor, inducing apoptosis in several neuronal populations (Kust et al., 2003; Pehar et al., 2006). p75NTR facilitates apoptosis during development and after injury to the CNS. Recent studies suggest that modulation of p75NTR by small molecule ligands targeting this receptor might constitute a novel strategy for preventing motor neuron degeneration (Pehar et al., 2006). Acute toluene administration in rats induces a significant increase in the numbers of neurons immunostained for p75NTR in several brainstem regions, such as the raphe magnus and the nucleus of the solitary tract, as well as in the lateral reticular, gigantocellular, vestibular and ventral cochlear nuclei, without any in the facial and spinal trigeminal nuclei and the dorsal horn of the spinal

cord. *These data suggest that p75NTR could be involved in toluene-induced neurotoxic effects as well as ALS (Pascual et al., 2004; Kust et al., 2003; Pehar et al., 2006).*

15. To counteract ROS- and electrophile-mediated injury, cells can induce a number of genes encoding phase II detoxifying enzymes and antioxidant proteins. The transcription factor nuclear factor-erythroid 2-related factor 2 (Nrf2) regulates the genetic expression of phase II detoxification enzymes such as glutathione-S-transferase and antioxidant proteins through an enhancer sequence referred to as the antioxidant-responsive element (ARE). Studies have shown that an increase in glutathione biosynthesis induced by Nrf2 activation in astrocytes prevents p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006) suggesting that modulating glutathione levels may alter the progression of ALS. It is important to note that glutathione levels are reduced in liver and brain regions from toluene-treated rats (Mattia et al., 1993).

16. As I have already discussed, ALS is associated with a loss of motor neurons. Exposures to neurotoxic chemicals can also kill motor neurons. It is therefore reasonable to expect that these two factors, which can independently kill neurons, might interact in some way. Simply put, if you need to kill 80% of the motor neurons you are born with in order to experience overt symptoms of ALS then any factor which can increase or decrease the natural progression of neuronal loss up to this critical point would be expected to decrease or increase the age at onset of ALS. With this in mind, pharmaceutical companies are working diligently to discover drugs that can prevent neuronal loss and thereby slow the progression of ALS. This work is contingent upon using *in vitro* screening studies (e.g. high-throughput electrophysiology) to identify possible candidate compounds based on the putative mechanisms involved in ALS as defined in the basic scientific literature. These "hits" are then tested and optimized in animal models of ALS before being approved for human clinical trials. Thus far, researchers have identified at least one compound rulizole, which is believed at this time to provide neuroprotection via inhibition of glutamate-mediated excitoxicity which can slow the progression of ALS.

17. A logical question when confronted with this knowledge is, "if a compound like rulizole can slow the progression of ALS can other compounds make it progress more rapidly"? Not surprisingly, the same *in vitro* studies used to identify "hits" in drug discovery studies and the same animal models used to optimize these hits before they are approved by the FDA for human use in Phase I clinical trials indicate that neurotoxicants such as toluene act in ways that would absolutely make them hasten the course of ALS. For example treatment of neurons with toluene (1 mM; 4 days) increased whole-cell responses to exogenously applied NMDA, reduced those evoked by GABA but did not alter responses generated by kainic acid. Immunoblot analysis revealed that toluene exposure increased levels of NR2A and NR2B NMDA receptor subunits with no change in NR1. Immunohistochemical analysis with confocal imaging showed that toluene-treated

neurons had significant increases in the density of NR1 subunits as compared with control neurons. Toluene exposure increased the amplitude of synaptic NMDA currents and decreased those activated by GABA. The results from this study suggest that exposure to toluene induces compensatory responses in the functional expression of ion channels that regulate neuronal excitability (Bale et al., 2005).

18. The pathogenesis of neurodegenerative diseases such as ALS most likely involves a genetic predispositions acting in concert with environmental insults. To test this hypothesis Andreassen and colleagues (2001) examined whether transgenic mice with the G93A mutation in Cu,Zn superoxide dismutase show increased vulnerability to either 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) or 3-nitropropionic acid (3-NP). Compared to littermate controls G93A transgenic mice showed a greater loss of striatal dopamine, DOPAC, and HVA at 50, 70, and 120 days of age following administration of MPTP; however, cell loss in the substantia nigra was not greater. The G93A transgenic mice showed significantly increased vulnerability to striatal lesions produced by 3-NP compared with littermate controls at 120 days of age. The finding that G93A mice show increased vulnerability to mitochondrial toxins further implicates mitochondrial dysfunction in the pathogenesis of neuronal death in these mice. *The findings support the hypothesis that a genetic defect can increase susceptibility to environmental toxins and that this may play a role in the pathogenesis of neurodegenerative diseases* (Andreassen et al., 2001).

19. In summary, I have presented the recognized and accepted mechanisms by which ALS is posited to cause the death of motor neurons. The well-recognized and important roles of oxidative stress and glutamatergic excitotoxicity are described in detail. I have defined the necessary terms for the reader so he or she can appreciate the materials presented herein. I have related this material to the current therapies for ALS for the purpose of demonstrating how chemicals can be used to positively alter the course of the disease.

J. Review of the Generally Accepted Mechanisms by which Toluene Causes Neurotoxicity

So, having examined the mechanisms by which neurodegeneration occurs in ALS, I now review the generally accepted means by which neurotoxic chemicals such as Toluene also cause neurodegeneration. First, I review Mr. Allen's chemical exposure.

1. Mr. Daniel Allen experienced an unwitting occupational exposure to neurotoxic chemicals in June of 2001 when the gym floor was being refinished at the college where he was employed. The refinishing process took one to two workweeks to complete. During the refurbishment process, Mr. Allen worked in his office, which was located just above the gym. He reportedly experienced acute symptoms of dizziness, headaches, and disorientation. Other people working in the area reported similar symptoms.

2. The Material Safety Data Sheets (MSDS) sheets provided by Martin flooring indicate that some of the products used in this process contained neurotoxic solvents. For example, the solvents contained in the Moisture Cure Coatings may cause damage to the nervous system with repeated or chronic exposures. Among the chemicals reportedly used during the refinishing of the gymnasium floor were the solvents methyl isobutyl ketone, xylene, toluene and Stoddard solvent (white spirit/mineral spirit). Although these solvents differ with respect to their individual neurotoxic potentials, exposure to mixtures of these chemicals increases the risk for neurotoxic effects. This is due in part to competitive inhibition of enzymes involved in detoxification process. Some of the compounds also share toxic mechanisms of action so their effects can be additive. More importantly the combined effects of exposures to compounds with different mechanisms of action can be even greater than the sum of their individual effects (synergism). The net result is that exposures to mixtures of neurotoxic compounds can result in adverse effects even when exposures limits for individual compounds have not been exceeded (Noraberg and Arlien-Soberg, 2000; Dobrev et al., 2002).

I will look at each of these chemicals (Stoddard Solvent, Xylene and Toluene) with an emphasis on the latter:

Stoddard Solvent

3. Stoddard solvent (white spirit/mineral spirit) is the most widely used solvent in the paint industry. Exposure to Stoddard solvent can cause dizziness and headaches. An increase in *oxidative stress has been associated with exposure to Stoddard solvent* (Lam et al., 1994).

Xylene

4. *Exposure to xylene has been associated with increased oxidative stress and a decrease in glutathione levels* (Pathirante et al., 1986; Piotrowska et al., 2002). Toluene and xylene are chemicals present in various laboratory and other industrial products. Their toxicity to the nervous system is well documented. The in vitro effects of toluene and xylene on the respiration of succinate-energized isolated rat liver mitochondria, membrane potential, Ca(2+) release, reactive oxygen species (ROS), and ATP levels as well as Ca(2+)-dependent, cyclosporine A-sensitive mitochondrial swelling, an indicator of mitochondrial permeability transition (MPT) have been studied. At 0.5-2.5 and 0.25-1mM concentrations respectively, toluene and xylene stimulated state 4 respiration in apparent association with mitochondrial membrane potential dissipation and Ca(2+) release; these actions of both solvents are consistent with mitochondrial uncoupling. At higher concentrations (2.5 and 5mM, respectively) toluene and xylene also inhibited state 3 respiration. At 0.1-1mM concentrations, xylene elicited significant increase of ROS generation and partly Ca(2+)-dependent cyclosporine A-sensitive mitochondrial swelling. At 1 mM concentration, toluene

or xylene caused depletions of mitochondrial ATP, amounting to 66.3% and 40.3%, respectively; depletions were only slightly dependent on Ca(2+). It was concluded that mitochondrial uncoupling via ATP depletion might be responsible for the cell toxicity of toluene described earlier and in particular, of xylene. In the case of xylene, mitochondrial ROS generation and MPT also appear to be involved (Revilla et al., 2007). Depletion of glutathione levels due to xylene exposure may also induce p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006).

Toluene

5. Toluene is a volatile organic solvent that is used in a variety of commercial, industrial and household products, including but not limited to adhesives, varnishes, lacquers, paints, and paint thinners. Exposure to toluene occurs in occupational and non-occupational situations. In addition toluene is commonly abused representing a significant worldwide health and social burden (Feldman, 1999). The Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for toluene is 200 ppm.. The OSHA Ceiling Concentration is 300 ppm (assessed as a 15-minute time weighted average exposure) and the maximum peak concentration above the acceptable ceiling concentration for an 8-hour shift is 500 ppm for a maximum duration of just 10 minutes (29 CFR 1910.1000).

6. A meta-analysis of the toluene data about shock avoidance behavior in rats and choice reaction time in humans suggests that a 10% change in rat avoidance behavior occurs at a blood concentration of toluene 25 times higher than the concentration at which a 10% change in human choice reaction time occurs. In contrast, in vitro studies of nicotinic acetylcholine receptors indicated that human and rat receptors do not differ in sensitivity to toluene. Analysis of other dose-response relationships for visual and cognitive functions in rats suggests that the apparent difference between rats and humans may be driven by the specific endpoints measured in the two species rather than by inherent differences in sensitivity to toluene (Bushnell et al., 2006).

7. Just like Mr. Allen, painters and other workers exposed to solvents such as toluene experience acute symptoms of dizziness, nausea, depression, and fatigue (Welch et al., 1991; Wang and Chen, 1993; Kishi et al., 1993). Brain magnetic resonance imaging shows cerebral and hippocampal atrophy as well as a loss in brain volume in toluene/solvent abusers as well as painters (Welch et al., 1991; Deleu and Hanssens, 2000; Kamran and Bakshi, 1998; Yamanouchi et al., 1995, Feldman et al., 1999).

8. "There seems to be a statistically significant association between work in the leather industry and subsequent development of motor neuron disease. The reason for this association may be occupational exposure to solvents, which may damage

motor neurons either directly or through activation of latent virus" (Hawkes et al., 1989).

9. Toluene is a known neurotoxicant used in lacquers, glues and paints. Exposure to toluene causes both reversible and irreversible changes in the central nervous system. The effects of toluene inhalation on some specific enzymes and glutamate and γ-aminobutyric (GABA) receptor expression and binding in defined parts of the rat brain have been studied following several exposure schemes (Williams et al., 2005).

10. As discussed above, the p75 neurotrophin receptor (p75NTR) is a member of the tumor necrosis factor receptor superfamily and acts as a death receptor, inducing apoptosis in several neuronal populations. Reduced p75NTR expression delays disease onset in female SOD1 transgenic mice (Kust et al., 2003). Improved survival in female mice was not correlated with increased motoneuronal survival, but with less astrocytic activation in lumbar ventral spinal cord, as shown by glial fibrillary acidic protein immunohistochemistry. Other studies have also shown that an increase in glutathione biosynthesis induced by Nrf2 activation in astrocytes prevents p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006). Importantly exposure to toluene induces a significant increase in the numbers of neurons immunostained for p75NTR in several brainstem regions of rats and depletes glutathione levels (Pascual et al., 2004). *These data demostrate that p75NTR is implicated in toluene-induced neurotoxic effects as well as in the progression of ALS (Pascual et al., 2004; Kust et al., 2003; Pehar et al., 2006).*

Glutathione Levels Implicated in ALS and Toluene Neurotoxicity

11. Glutathione (GSH) is an extremely important cellular protectant. It directly quenches reactive hydroxyl free radicals, other oxygen-centered free radicals, and radical centers on DNA and other biomolecules. Glutathione is synthesized in the body from 3 amino acids: Cysteine, glutamine and glycine. Cysteine is one of the sulfur containing amino acids used for the synthesis of glutathione. N-Acetyl Cysteine (NAC) is the rate limiting amino acid for the production of glutathione within the cells of the body and it too is a powerful antioxidant and detoxifier. The thiol group is the active part of the molecule and serves as a reducing agent to prevent oxidation of tissues. Glutathione acts as one of the major detoxifiers in the body, but it must be in the *reduced form* to work properly. The unreduced form isn't metabolically active. Riboflavin, niacinamide, selenium, lipoic acid and glutathione reductase are all essential cofactors for generating *reduced glutathione*. When reduced GSH loses electrons the molecule becomes oxidized, and two such oxidized GSH molecules can linked together (dimerized) by a disulfide bridge to form glutathione disulfide or oxidized glutathione (GSSG). This linkage is reversible upon re-reduction. GSH is under tight homeostatic control both intracellularly and extracellularly. A dynamic balance is maintained between GSH synthesis, its recycling from GSSG/oxidized glutathione, and its utilization. GSH synthesis involves two closely linked enzymatically controlled

reactions that utilize ATP. First cysteine and glutamate are combined, by gamma-glutamyl cysteinyl synthetase. Second, GSH synthetase combines gamma-glutamylcysteine with glycine to generate GSH. As GSH levels rise, they self-limit further GSH synthesis; otherwise, cysteine availability is usually rate-limiting. GSH recycling is catalyzed by glutathione disulfide reductase, which uses reducing equivalents from NADPH to reconvert GSSG to 2GSH.
Direct attack by free radicals and other oxidative agents can deplete GSH. The homeostatic glutathione redox cycle attempts to keep GSH repleted as it is being consumed. Amounts available from foods are limited (less than 150 mg/day) and thus oxidative depletion can easily outpace synthesis.

12. A motor neuron-like cell culture system and a transgenic mouse model have been used to study the effect of cellular GSH levels on motor neuron cell death. Exposure of NSC34 motor neuron-like cells to ethacrynic acid (EA) or l-buthionine sulfoximine (BSO) dramatically reduced the cellular GSH levels, and was accompanied by increased production of reactive oxygen species (ROS) measured by the dichlorofluorescin (DCF) fluorescent oxidation assay. In addition, depletion of GSH enhanced oxidative stress markers, AP-1 transcriptional activation, c-Jun, c-Fos and heme oxygenase-1 (HO-1) expression in NSC34 cells analyzed by a luciferase reporter, Western blotting and quantitative PCR assays respectively. Furthermore, depletion of GSH decreased mitochondrial function, facilitated apoptosis inducing factor (AIF) translocation, cytochrome c release, and caspase 3 activation, and consequently led to motor neuron-like cell apoptosis. In an ALS-like transgenic mouse model overexpressing mutant G93A-Cu, Zn-superoxide dismutase (SOD1) gene, it was shown that the reduction of GSH in the spinal cord and motor neuron cells is correlated with AIF translocation, caspase 3 activation, and motor neuron degeneration during ALS-like disease onset and progression. *Taken together, the in vitro and in vivo data presented in the current report demonstrated that decreased GSH promotes multiple apoptotic pathways contributing, at least partially, to motor neuron degeneration in ALS* (Chi et al., 2007).

13. Animal studies have demonstrated that toluene reduces GSH levels (Mattia et al., 1993). Workers exposed to benzene, toluene, xylene, hexane, ethylbenzene have significantly lower GSH concentrations ($p < 0.001$) compared to unexposed controls (Georgieva et al., 2002).

Oxidative Stress and Phase II Metabolic Enzymes Implicated in ALS and Toluene Neurotoxicity

Plasma malondialdehyde (MDA, a product of lipid peroxidation) levels and activity levels of the antioxidant enzymes gluthatione peroxidase (GSH-Px) and superoxide dismutase (SOD) in erythrocytes of people ($n = 18$) working with paint thinner containing toluene were ascertained as indicators of oxidative stress. Glutathione peroxidase is a compound involved in detoxification against peroxides and other xenobiotics. It is synthesized from selenium and cysteine.

14. The control group was composed of 18 healthy adults. There was a significant ($p < 0.001$) increase in plasma MDA levels and GSH-Px activity levels in people working with paint thinner compared with control subjects. Similarly, there was also an increase ($p < 0.05$) in the SOD levels of people working with paint thinner compared with controls. These observations suggest that paint thinner inhalation increases lipid peroxidation and consequently induces synthesis of antioxidant enzymes in an attempt to prevent damage to at risk cells (Halifeoglu et al., 2000).

15. Feldman and Ratner (1999) proposed that exposures to neurotoxicants interact with genetic predispositions that modify the ability of the body to metabolize and detoxify chemicals such that the clinical course of a neurodegenerative disease is hastened. Recently the interaction between neurodegenerative disease and genetics that my colleague and I predicted based on our expertise in this area at the time was confirmed by a Boston University study looking at the genes involved in the metabolism of toxic chemicals and age at onset of the neurodegenerative disease Parkinson's disease (Wilk et al. 2006). In this study Wilk and colleagues found an interaction between certain genes that encode for the enzyme glutathione-*S*-transferase and a younger age at onset of PD among persons exposed to herbicides. These findings and others contribute to the growing body of literature demonstrating that genetics factors can interact with exposures to chemicals to alter the clinical course of neurodegenerative diseases such as ALS and Parkinson's disease.

16. *Glutathione S-transferase* is an enzyme responsible for inactivation of a large variety of toxic electrophilic compounds and organic peroxides. GST activity and GST pi expression were also studied in patients with amyotrophic lateral sclerosis (ALS). Studies were conducted on cerebrospinal fluid (CSF), blood serum and peripheral blood mononuclear cells (PBMC) obtained from 40 ALS patients. CSF from 30 subjects without neurological diseases and blood from 40 healthy blood donors were used as controls. GST activity assayed with 1-chloro-2,4-dinitrobenzene (substrate for transferase activity) and cumene peroxide (substrate for peroxidase activity) was significantly decreased in PBMC of ALS patients, as well as the GST pi expression on both mRNA and protein level. The mean peroxidase activity was however significantly increased in CSF and serum of ALS patients with the specificity of 80% and 73%, and the sensitivity of 78% and 85%, respectively. *It can thus be concluded that the protective effect provided by GST is reduced in peripheral blood of ALS patients, and may increase their vulnerability to toxic effects of electrophilic compounds and organic peroxides.* Studies on a larger group are needed to answer the question whether GSH-Px determination may be implicated in the diagnosis of ALS (Kuzma et al., 2006).

17. The expression of the pi isozyme of glutathione-S-transferase (GST pi) was studied in spinal cord, motor and sensory brain cortex obtained from patients who died in the course of amyotrophic lateral sclerosis (ALS). The studies were performed on formalin-fixed, paraffin-embedded (FFPE) and freshly frozen tissues. The method of RNA isolation from FFPE was modified. A significant

decrease of GST pi-mRNA expression was found in cervical spinal cord and motor brain cortex of ALS subjects comparing to analogue control tissues ($P<0.01$), as well as in motor cortex of ALS subjects comparing to their sensory cortex ($P<0.05$). In spinal cords the decrease in GST pi-mRNA expression was accompanied by a decrease of GST pi protein level. *Results indicated lowered GST pi expression on both mRNA and protein levels in the regions of the nervous system affected by ALS. The non-properly inactivated by GST toxic electrophiles and organic peroxides may thus contribute to motor neurons damage* (Usarek et al., 2005).

18. Toluene and its metabolites have been studied with respect to their reactive oxygen species-enhancing potential in isolated systems and in vivo. The induction of reactive oxygen species (ROS) production was assayed in this study using the probe 2',7'-dichlorodihydrofluorescin diacetate (DCFH-DA). Intraperitoneal injection of toluene, benzyl alcohol or benzaldehyde caused a significant elevation in the rate of ROS formation within hepatic mitochondrial fractions (P2). In the brain, only toluene induced ROS formation, while benzyl alcohol and benzaldehyde did not have any effect. Glutathione (GSH) levels were depressed in liver and brain regions from toluene-treated rats. However, no such depression was evident in brains treated with toluene metabolites. P2 fractions from phenobarbital-pretreated rats exhibited a heightened ROS response when challenged with toluene, in vitro. Pretreatment of rats in vivo with 4-methylpyrazole, an alcohol dehydrogenase inhibitor, or sodium cyanamide, an aldehyde dehydrogenase inhibitor, prior to exposure to toluene, caused a significant decrease and increase, respectively, in toluene-stimulated rates of ROS generation in the CNS and liver. Electron spin resonance spectroscopy, employing the spin trap 5,5-dimethyl-1-pyrroline N-oxide (DMPO), was conducted. Incubation of the spin trap with P2 fractions and toluene or benzaldehyde elicited a spectrum corresponding to the hydroxyl radical. Incubation of benzaldehyde with aldehyde dehydrogenase produced a strong signal that was blocked completely by superoxide dismutase and inhibited partially by catalase, suggesting the presence of superoxide radicals and the involvement of the iron-catalyzed Haber-Weiss reaction leading to the production of hydroxyl radicals. Thus, ROS generation during toluene catabolism may occur at two steps: cytochrome P450 oxidation and aldehyde dehydrogenase oxidation. In addition, GSH may play an important role in protection against the induction of ROS generation in the CNS and liver following exposure to toluene (Mattia et al., 1993) as well as in p75NTR-dependent motor neuron apoptosis (Vargas et al., 2006) as previously cited.

19. The following study was designed to investigate the effects of chronic toluene inhalation in high concentration on lipid peroxidation, antioxidant enzyme activities and ultrastructural changes in the sciatic nerves of rats. Male Wistar albino rats (150-250 g) were divided in two experimental groups: the control and the toluene treated group ($n = 10$ for each). Toluene treatment was performed by inhalation of 3000 ppm toluene, in a 8 h/day and 6 day/week order for 16 weeks.

Blood and tissue samples were obtained for biochemical and histopathological investigation. The blood and sciatic nerves were assayed for toluene by gas chromatography. Toluene significantly increased blood and tissue malondialdehyde (MDA), and decreased tissue superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), but not tissue catalase (CAT) levels when compared with controls. Electron micrographs of sciatic nerve in the toluene group shows myelin destructions with onion-bulb and bubble form protrusion on the myelin sheath and axolemma border of myelinated axons. The area of injury on the myelin sheath were measured by Image-Pro Plus. Mean of the injury area were estimated 34% each myelin. These findings indicate that chronic toluene inhalation might be involved with free radical processes (Coskun et al., 2005).

20. The following study investigated glial reactivity in hippocampus, cortex and cerebellum and the expression of glial fibrillary acidic protein (GFAP) after exposure of rats to toluene vapor (3000 ppm) for 45 days. The protective effects of melatonin whish is neuroprotective against free radical damage was also examined. Western blots demonstrated a marked elevation in total Glial Fibrillary Acidic Protein (GFAP), a specific marker for astrocytes, induced by thinner fume inhalation in the hippocampus ($P<0.001$), cortex ($P<0.01$) and cerebellum ($P<0.05$) of rats. Melatonin administration prevented the increase of total GFAP induced by thinner fume inhalation. Thinner exposure caused a significant increase of lipid peroxidation products (malondialdehyde and 4-hydroxyalkenals) in all brain regions ($P<0.01$ for each region), and this elevation was also was inhibited by melatonin. Furthermore, melatonin augmented glutathione levels in all brain regions ($P<0.05$ for each region) investigated. In conclusion, melatonin treatment may provide neuroprotection against toluene neurotoxicity by increasing the survival of glial cells possibly by directly scavenging ROS and by indirectly augmenting their antioxidant capacity (Baydas et al., 2003).

21. Bjornaes and Naalsund, (1988) studied the activities of the transmitter synthesizing enzymes glutamic acid decarboxylase (GAD), choline acetyltransferase (ChAT) and aromatic amino-acid decarboxylase (AAD) as markers for permanent loss of neuronal activity. Catecholaminergic neurons showed a 50% reduction in the brainstem after 4 weeks of exposure to 250 and 1000 ppm toluene. Following 500 ppm of toluene, 16 h/day for 3 months, a general increase in the activities was seen. This is most probably due to a reduction in total protein content, to which the activities were related. The neurotransmitters glutamate and GABA had their specific receptor binding increased in most of the brain areas studied, but decreased in some areas. The glial enzyme, glutamine synthetase, had its activity increased in the cerebellar hemisphere following 4 weeks exposure to 1000 ppm. This suggests that glial cells in the area may have proliferated, a frequent phenomenon following CNS damage (Bjornaes and Naalsund, 1988).

Toluene Mediated Effects on Neurotransmission Implicated in ALS

22. The acute effects of toluene are due to pharmacological mechanisms that are similar to other CNS depressants such as 1,1,1-trichloroethane. Acute exposure to toluene is associated with anticonvulsant and anxiolytic effects (Bowen et al., 1996; Lopez-Rubalcava et al., 2000) and has discriminative stimulus properties that are similar to those of ethanol (Rees et al., 1987a), pentobarbital (Rees et al., 1987b) and diazepam (Bowen et al., 1999). Suggesting that it like other CNS depressants produces effects in part by modulation of neuronal firing. Toluene and other abused inhalants such as 1,1,1-trichloroethane have been shown to potentiate the function of $GABA_A$ receptors expressed in *Xenopus* oocytes (Mihic et al., 1997; Beckstead et al., 2000).

23. To investigate the effects of acute toluene exposure on the amino acid neurotransmitter levels in the hippocampus, an *in vivo* microdialysis study was performed in freely moving mice after a single intraperitoneal administration of toluene (150 and 300 mg/kg). Amino acid neurotransmitters in microdialysates were measured by a high performance liquid chromatography system. The extracellular levels of glutamate and taurine were rapidly and reversibly increased within 30 min after the toluene administration in a dose-dependent manner and returned to the basal level by 1h. Conversely, the extracellular level of glycine and GABA were stable, and no significant change was observed after the toluene administration. To further investigate the brain toluene level in the hippocampus of toluene-administered mice, a solid-phase microextraction (SPME) method was used and the time course changes of toluene in the hippocampus of living mice were examined. The brain toluene level reached the peak at 30 min after injection and returned to the basal level after 2h and the relationship between brain toluene levels and amino acid neurotransmitter glutamate and taurine levels in the hippocampus was observed. These findings suggest that toluene glutamatergic and taurinergic neurotransmission in the hippocampus of freely moving mice possibly by increasing neurotransmitter release (Win-Shwe et al., 2007).

24. There is also evidence indicating that toluene modulates the activity of ionotropic glutamate receptors. Toluene has also been demonstrated to produce phencyclidine-like discriminative stimulus effects (Bowen et al., 1999), suggesting that it may acutely inhibit *N*-methyl-D-aspartate (NMDA) receptors. In vitro studies using *Xenopus* oocytes transfected with heterologous recombinant NMDA receptors, toluene rapidly and reversibly inhibits receptor function (Cruz et al., 1998). These studies assessed the effects of toluene on the electrophysiological function of NMDA receptors containing NR1 subunits in combination with NR2A, NR2B or NR2C subunits. Of these, the NR1/2B combination was the most sensitive to the inhibitory effects of toluene while other non-NMDA receptor subunits were less sensitive. These studies suggest that toluene may produce some of its effects by directly modulating NMDA receptor function in a subunit-selective manner.

25. The pharmacologic effects of toluene may be inhibitory or excitatory. Of equal concern is the observation that toluene activates signal transduction pathways that regulate expression of GABA and glutamate receptors. Exposure to toluene has been associated with an increase in the incidence of temporal lobe epilepsy and decrease in IQ scores (Byrne et al., 1991). The mechanism associated with these changes in seizure susceptibility and cognitive function appear to involve toluene induced alterations in receptor sybtype expression. Toluene increases expression of the alpha1 subunit of the $GABA_A$ receptor and of the NR1, NR2B and GluR2/3 subunits of the glutamate receptors in the medial prefrontal cortex. Decreased $GABA_A$ alpha1 and glutamate NR1 subunits expression was seen in the substantia nigra pars compacta. Toluene inhalation produced modest increases in $GABA_A$ alpha1 subunits in the striatum, as well as slight decreases in the expression of this subunit in the ventral tegmental area. NR2B subunit levels were slightly increased within the nucleus accumbens by toluene. These studies show that toluene differentially alters the levels of specific $GABA_A$ and glutamate receptor subunits in a regionally selective manner (Williams et al., 2005). These changes in receptor expression can predipopse the individual to seizures and to excitotoxicity. ICR mice exposed to 250 ppm toluene via inhalation for four days developed mild dependence upon termination that was characterized by an increase in severity of handling-induced convulsions (Wiley et al., 2003). The effects of toluene on the sensitivity to seizures induced by aminophylline has also been investigated in mice. Toluene increased seizure susceptibility to aminophylline in a dose- and time-dependent manner. Toluene-induced enhancement of seizure susceptibility to aminophylline occurred as early as 30 min and persisted for at least 3 days after a single administration of toluene (500 mg/kg) (Chan and Chan, 2003). *These observations are extremely important since they indicate that toluene makes neurons more vulnerable to excitation and thus to excitotoxicity.*

26. When a glutamatergic motor neuron dies (irrespective of why it dies) it releases glutamate into the extracellular space. This glutamate is free to act on adjacent motor neurons and cause these cells to experience an increase in calcium influx that ultimately leads to cell death. As each adjacent neuron dies the amount of glutamate in the extracellular space increases. This promotes a vicious excitotoxic cascade that perpetuates the loss of neurons.

27. Compounds that inhibit glutamaterigic neurotransmission are promising candidates as therapeutics for ALS. Unfortunately, the cell's own machinery is genetically predisposed to modulate glutamatergic neurotransmission at a set level for optimum brain function. As a result, the cells quickly override this pharmacologic effect by generating more glutamate receptors, which actually increases the risk of excitoxicity. As a result the clinical efficacy of compounds such as rulizole is limited at best. The recommendation that rulizole not be stopped abruptly once therapy is initiated is related to this phenomenon. Since the cells are naturally trying to combat the effect of the drug, abruptly stopping it

leaves the cells in an up-regulated state and therefore even more vulnerable to the excitotoxic effects of glutamate.

Apoptosis and Toluene

28. *In vitro* and *in vivo* data suggest that decreased GSH promotes multiple apoptotic pathways contributing, at least partially, to motor neuron degeneration in ALS (Chi et al., 2007). It has been shown that the inhalation of toluene in rats can cause neuronal apoptosis in the central nervous system. However, the cellular and molecular effects of toluene directly on astrocytes are not well studied. The following study used primary cultures of astrocytes isolated from the neonatal rat cortex as a model to study the toluene effects on cell outcome and associated signal transduction pathways using immunostaining and Western blotting. Acute toluene exposure significantly induced caspase-dependent cell apoptosis and transiently stimulated the activation of p42/44 mitogen-activated protein kinase (MAPK) in the primary astrocytes. Interestingly, the inhibition of the p42/44 MAPK signaling cascade by PD98059 in conjunction with the toluene treatment evoked more cellular apoptosis than toluene alone, suggesting that the toluene-induced transient MAPK activation may play a role in promoting cell survival during the toluene exposure (Lin et al., 2002).

29. To study the cytotoxicity of toluene and its mechanism, hippocampal neurons were cultured and exposed to toluene *in vitro*. The neurons from newborn SD rat's hippocampus were primarily cultured for two weeks, then administered with toluene (3, 6, 9 mmol/L), with blank control group and excipient group being also set up. 24 hours later, Morphology and viability of the cells, the LDH activity, [Ca2+]i, and cell apoptosis were examined. Protuberances of neurons of the toluene-exposed groups were damaged; the bodies of the neurons became round and swollen; the number of the cells decreased; the LDH activity of neurons of high-dose group increased significantly compared with control group ($P < 0.05$). [Ca2+]i of toluene-exposed groups also increased significantly compared with control group($P < 0.05$) in a dose-dependent manner; after diltizem as antagonist of calcium tunnel was added, no increase of [Ca2+]i was found; and evident apoptosis of the exposed cells were also found. Toluene was toxic to the neurons after being administered *in vitro*, which might be ascribed to higher lipid solubility of toluene and it's ability to increase calcium influx, the latter facilitating apoptosis (Yan et al., 2004).

30. The mechanisms underlying the acute neurophysiological and behavioral effects of volatile organic compounds (VOCs) remain to be elucidated. However, the function of neuronal ion channels is perturbed by VOCs. The present study examined effects of toluene (TOL), trichloroethylene (TCE), and perchloroethylene (PERC) on whole-cell calcium current (ICa) in nerve growth factor-differentiated pheochromocytoma (PC12) cells. All three VOCs affected ICa in a reversible, concentration-dependent manner. At +10-mV test potentials, VOCs inhibited ICa, whereas at test potentials of -20 and -10 mV, they

potentiated it. The order of potency for inhibition (IC50) was PERC (270 microM) > TOL (720 microM) > TCE (1525 microM). VOCs also changed ICa inactivation kinetics from a single- to double-exponential function. Voltage-ramp experiments suggested that VOCs shifted ICa activation in a hyperpolarizing direction; this was confirmed by calculating the half-maximal voltage of activation (V1/2, act) in the absence and presence of VOCs using the Boltzman equation. V(1/2, act) was shifted from approximately -2 mV in control to -11, -12, and -16 mV by TOL, TCE, and PERC, respectively. Similarly, VOCs shifted the half-maximal voltage of steady-state inactivation (V1/2, inact) from approximately -16 mV in control to -32, -35, and -20 mV in the presence of TOL, TCE, and PERC, respectively. Inhibition of ICa by TOL was confirmed in primary cultures of cortical neurons, where 827 microM TOL inhibited current by 61%. These data demonstrate that VOCs perturb voltage-sensitive Ca2+ channel function in neurons, an effect that could contribute to the acute neurotoxicity of these compounds (Shafer et al., 2005)

31. Chronic toluene inhalation at concentrations above occupational exposure limits (e.g., 100 ppm; NIOSH) has been repeatedly shown to induce neurotoxic effects. In contrast, although few clinical and experimental data are available on the effects of toluene exposure at concentrations below occupational exposure standards, some of these data may support adverse effects of long-term exposure to low toluene concentrations. To test this hypothesis, Berenguer et al., (2003) investigated the neurobehavioral and neurochemical effects of 40 ppm inhaled toluene in a rat model of 16-week subchronic exposure, examining locomotor and rearing activities; adaptation/sensitization to narcosis produced by acute exposure to toluene at high concentration; and tyrosine hydroxylase and tryptophan hydroxylase activities, and dopamine (DA) and serotonin (5-HT) turnovers in the caudate-putamen, nucleus accumbens, hippocampus, prefrontal cortex, and cerebellum. The results of this study mainly show that subchronic exposure to 40 ppm toluene resulted in sensitization to toluene-induced narcosis, a decrease in rearing activity, and alterations in DA and 5-HT neurotransmission. *This demonstrates that subchronic toluene exposure at a low concentration may lead to adverse changes in neurobehavioral and neurochemical functioning, and further questions in a public health perspective the actual neurotoxic potential of toluene and other organic compounds, because deficits in functioning are generally viewed as precursors of more serious adverse effects* (Berenguer et al., 2003).

32. Gotohda et al., (2006) from the Department of Forensic Medicine, Institute of Health Biosciences, The University of Tokushima Graduate School, in Tokushima, Japan investigated the effects of toluene inhalation on neurons and neurotrophic factors in the spinal cord and the relationship between them. Male Wistar rats were exposed to toluene (1500ppm for 4h per day) for 7 days. To observe damage of the neurons in spinal cord due to toluene, expression of microtubule associated protein 2 (MAP2) and 70kDa heat shock protein (HSP70) were determined by immunohistochemistry. MAP2 was degraded and HSP70-

immunoreactivity was enhanced in nerve cell bodies of the gray matter in toluene inhalation group. Immunoreactivity of glial fibrillary acidic protein (GFAP), a marker of astrocytes, was enhanced in the toluene-treated group. Furthermore, glial cell line-derived neurotrophic factor (GDNF)- and brain-derived neurotrophic factor (BDNF)-immunoreactivity in spinal cord were slightly decreased in the treated group. In addition, the concentrations of GDNF and BDNF in the spinal cord were determined using enzyme linked immunosorbent assay (ELISA). Concentration of GDNF was reduced significantly by toluene exposure. BDNF also reduced, but not significantly. The toluene inhalation caused damage to neurons in the spinal cord, which was accompanied by a decrease in the neurotrophic factors, such as BDNF and GDNF (Gotohda et al., 2006). MAP2 expression decreased in the anterior gray horn of all ALS cases and in the intermediate gray of several ALS cases. This reduction was correlated with the degree of degeneration and neuronal loss in anterior horn cells and with the clinical symptoms of limb weakness (Kikucki et al., 1999). *These observations provide compelling support for the interaction between exposure to toluene and the progression of ALS.*

33. In summary, I have presented the mechanisms by which toluene is posited to cause the death of neurons. Whenever possible I have provided data related to the effects of toluene on motor neurons specifically. I have defined the necessary terms so the reader can follow the materials presented herein. I have related this material to the mechanisms of neuronal loss implicated in ALS and to the current therapies for ALS specifically for the purpose of demonstrating how chemicals can negatively alter the course of the disease. I have provided an extensive review of the literature to provide the reader with sufficient data to appreciate that toluene exposure is associated with oxidative stress and glutamatergic excitotoxicity both which as described above have also been very strongly implicated in the pathogenesis of ALS.

K. Dan Allen's Level of Exposure to Toluene

1. The Occupational Safety and Health Administration (OSHA) considers toluene to be a toxicant. The current OSHA Permisible Exposure Limit for toluene is 200 ppm TWA; Also, exposures shall not exceed 300 ppm (15 minute TWA ceiling) with the following exception: exposures may exceed 300 ppm, but not more than 500 ppm (peak), for a single time period up to 10 minutes for any 8-hour shift. (29 CFR 1910.1000).

2. According to the OSHA "before a worker is placed in a job with a potential for exposure to toluene, a licensed health care professional should evaluate and document the worker's baseline health status with thorough medical, environmental, and occupational histories, a physical examination, and physiologic and laboratory tests appropriate for the anticipated occupational risks. These should concentrate on the function and integrity of the central nervous system and skin. A preplacement medical evaluation is recommended to assess an

individual's suitability for employment at a specific job and to detect and assess medical conditions that may be aggravated or may result in increased risk when a worker is exposed to toluene at or below the prescribed exposure limit. The health care professional should consider the probable frequency, intensity, and duration of exposure as well as the nature and degree of any applicable medical condition. Such conditions (which should not be regarded as absolute contraindications to job placement) include a history and other findings consistent with diseases of the central nervous system or skin."
(http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html)

3. OSHA has reviewed the literature and noted the following acute effects of exposure to toluene: "Volunteers exposed to a 200-ppm concentration of toluene for 8 hours experienced mild upper respiratory tract irritation; at 400 ppm, subjects experienced mild eye irritation and tearing and laughed inappropriately; at 600 ppm, the volunteers developed slight nausea and lassitude; and at 800 ppm, they experienced drowsiness, incoordination, and a metallic taste in the mouth [Clayton and Clayton in Patty's Industrial Hygiene and Toxicology, 1981-1982, p. 3283; Hathaway, Proctor, Hughes, and Fischman, Proctor and Hughes' chemical hazards of the workplace. 1991, p. 546]."
(http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html)

4. Echeverria et al., 1989 noted subtle acute effects to be associated with exposure to toluene at just below (75 ppm) and above (150 ppm) the OSHA PEL of 100 ppm supporting the position that the guideline be lowered since the biological threshold of behavioral effects may be comparable with the TLV. It should be noted the OSHA PEL of 100 ppm was vacated on July 7, 1992, in accordance with the U.S. Court of Appeals, Eleventh Circuit, ruling which vacated the 1989 PELs listed in the "Final Rules" columns of Table Z-1-A of 29 CFR 1910.1000.

5. Mr. Allen and his coworkers reported symptoms that included dizziness, nausea and headaches. Based on these reported symptoms and the results of the findings reported in the studies cited by OSHA, Mr. Allen had to have been exposed to concentrations that at least exceeded the OSHA PEL, established to protect workers against the health effects of exposure to hazardous substances. In addition, Mr. Allen who we now know had latent ALS at the time of his exposure did not receive medical clearance before he was exposed to toluene and other chemicals used in the floor refurbishment process as recommended by OSHA. (http://www.osha.gov/SLTC/healthguidelines/toluene/recognition.html)

L. My Case Specific Causation Assessment

I have used the data presented herein to formulate my conclusions regarding causation in this case. To arrive at this conclusion:

1. I first compiled a list of acute complaints and symptoms and related these chronologically to all possible occupational and non-occupational sources of chemical exposures.

2. I have noted the time of onset, duration, and intensity of the acute complaints and indicated when symptoms worsen or remit in relation to exposure (e.g. work week, week end, time of shift, on vacation).

3. I have evaluated Mr. Allen's family/genetic health, special sensitivities, and possible congenital factors.

4. I have identified the chemicals Mr. Allen was exposed to and how these were used.

5. Whenever possible, I have obtained chemical names (not trade label names), material safety data sheets, and other identifying data concerning each substance.

6. I have reviewed the workplace information provided regarding ventilation systems and floor plans.

7. I have attempted to obtain environmental and industrial hygiene air measures to prove the presence of alleged chemicals in the alleged source.

8. I have attempted to obtain urine and/or blood samples from the affected individual to establish body burden of chemical. Although these measures were not available in this case, there is nevertheless sufficient evidence based on acute symptoms of exposure reported by Mr. Allen and others along with the documentation of the events to conclude that a substantial exposure to the chemicals identified did occur.

9. I have obtained information on dose-response relationships, animal studies, toxicological and epidemiological studies for the chemicals cited.

10. I have confirmed the subject's complaints by a clinical neurological examination, neurophysiological tests, and, appropriate blood and urine analyses.

11. I have differentiated these findings from those seen in idiopathic primary neurological disease.

12. I have attempted to find alternative explanations based on the findings of past medical history, previous and/or current unrelated exposures to substances from sources other than the one under consideration.

13. I have identified and critically reviewed previously published and/or reported case reports, case control studies, population studies, and animal studies concerning the alleged neurotoxicants and related this to the case specific data.

14. I have considered all of this information collectively in arriving at my opinion. It is my professional opinion based on my training and experience that there is sufficient data in this case to arrive at the following conclusions with a reasonable degree of scientific certainty.

M. Conclusion

1. ALS is a progressive neurodegenerative disorder associated with loss of motor neurons that is mediated by in part by oxidative stress and in part by glutamate mediated excitotoxicity which collectively lead to cell death via induction of apoptosis (programmed cell death). These two mechanisms each play important roles in the onset and progression of the disease.

2. Mechanisms that prevent either oxidative stress or glutamate mediated excitotoxicity are useful in delaying the onset and slowing the progression of ALS in both animal models and in humans.

3. It logically follows that exposure to chemicals that increase oxidative stress or glutamate-mediated excitotoxicity will hasten both the onset and the clinical course of ALS. Furthermore, a researcher would have to ignore the scientific method of reasoning to hypothesize otherwise.

4. Mr. Allen and his coworkers reported exposures to chemicals at concentrations that were at least high enough to cause acute symptoms including dizziness, nausea and headaches.

5. It can therefore be concluded with a reasonable degree of medical certainty that the exposures were high enough to alter neuronal functioning since dizziness is a symptom of this.

6. My review of the materials provided indicates that

- Mr. Allen was exposed to neurotoxic chemicals during the refurbishment of the gym floor;
- Mr. Allen's experienced symptoms consistent with disruption of normal neurological function during his exposure;
- Mr. Allen developed symptoms of ALS in chronological relationship to this specific exposure event;
- Mr. Allen had no family history of ALS which typically develops earlier in life than sporadic ALS but also runs a slightly longer course (According to a report by authors from the Laboratory of Central Nervous System Studies, National Institutes of Health, the age-dependent incidence of sporadic ALS, the age of onset of familial ALS is normally distributed about a mean of 45.7 years-old (Strong et al., 1991; Norris et al., 1993); and 5) that his first overt symptoms of ALS emerged when he was only 45-years-old.

7. ALS is general considered to be a disease of middle to late life. Published reports indicate that the average age at onset for non-familial sporadic ALS is 60 years-old (Sorenson et al., 2002; Norris et al., 1993; Juergens et al., 1980).

8. These observations indicate that Mr. Allen developed the disease much earlier than would be expected based on his negative family history and the epidemiological findings (Sorenson et al., 2002; Chio et al., 2002).

9. There is also sufficient evidence to support the conclusion that the exposure to Toluene and other chemicals was a substantial contributory factor in the age at onset of the disease since there was no reported family history of the disease, the age at onset was atypical, the onset occurred after the exposure event, and several of the chemicals Mr. Allen was exposed to are known to be neurotoxic (e.g., toluene).

10. It can therefore be concluded with a reasonable degree of medical certainty that Mr. Allen would have been unlikely to develop overt symptoms of ALS at age 45-years-old and would not have died on May 16, 2004 had he not been exposed to the chemicals used in the gym floor refurbishment process.

11. I hold all of the opinions in this report to a reasonable degree of scientific certainty. I reserve the right to further supplement this report and respond to the reports submitted by the defense.

Marcia Ratner, Ph D.

Dated: June 14 2007

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UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION NO. 05-40048-FDS

RULE 26 SUPPLEMENTAL EXPERT REPORT – DR. MARCIA RATNER

Dr. Ratner supplements her initial report dated June 14, 2007, as follows:

I recently became aware of a peer-reviewed paper by Morahan JM, et al., entitled "Genetic susceptibility to environmental toxicants in ALS", which was published (online) on May 14, 2007 in the American Journal of Medical Genetics (Wiley-Liss, Inc).

This paper is not cited by defense expert Hashimoto.

The Morahan paper is one additional piece of scientific evidence which supports my opinion that the solvents to which Coach Allen was exposed are capable of accelerating the onset of sporadic ALS. The Morahan paper is an observational genetics study, whose findings "suggest that environmental toxicants, and genetic susceptibilities to these toxicants, play a role in some cases of [sporadic ALS]".

While the Morahan paper has limitations (as do all studies) and while this study alone does not prove causation (as is the case with all single studies for the reasons I've explained in my June 14, 2007 report), it adds to, and supports my opinions with regard both to causation and the mechanism of action at issue.

As the authors note (consistent with my initial disclosure), glutathione is involved in the detoxification process and disruption of this pathway could adversely impact the ability of the body to cope with exposure to neurotoxic solvents, thereby increasing the risk of ALS.

The Morahan paper is enclosed here.

I hold all of the opinions in this report to a reasonable degree of scientific certainty. I reserve the right to further supplement this report and respond to the reports submitted by the defense.

Marcia H. Ratner, Ph.D.

Dated: September 10, 2007

CURRICULUM VITAE

DATE PREPARED: June 15, 2007

Part I:

DEMOGRAPHIC INFORMATION:

Name: L. Christine Oliver
Address: 1101 Beacon Street
Four West
Brookline, MA 02446
Place of Birth: Raleigh, North Carolina

EDUCATION and TRAINING:

Education:

1966	AB	University of North Carolina, Chapel Hill, NC
1970	MD	University of North Carolina School of Medicine, Chapel Hill, NC
1978	MPH	Harvard School of Public Health, Boston, MA
1979	MS	Harvard School of Public Health, Boston, MA

Postdoctoral Training:

1970-1971	Internal Medicine North Carolina Memorial Hospital, Chapel Hill, NC
1972-1974	Social Medicine/Internal Medicine Montefiore Hospital, Bronx, NY
1977-1979	Occupational Medicine Harvard School of Public Health, Boston, MA

Licensure and Certification:

1970	North Carolina License, Medicine, Certificate #03484
1974	New York License, Medicine, Certificate #119861
1975	Massachusetts License, Medicine, Certificate #38968
1974	American Board of Internal Medicine, Certification
1982	American Board of Preventive Medicine, Certification
1980	National Institute of Occupational Safety and Health (NIOSH) "B" Reader Certification Occupational Pneumoconioses
1985, 1989, 1993, 1997, 2001	NIOSH "B" Reader Recertification

PROFESSIONAL APPOINTMENTS:

Academic Appointments:

1974-1975	Assistant Professor of Medicine, Albert Einstein School of Medicine, Bronx, NY
1976-1979	Instructor in Medicine, Harvard Medical School, Boston, MA
1980-1982	Clinical Instructor in Medicine, Harvard Medical School
1982-1986	Instructor in Medicine, Harvard Medical School
1986-1998	Assistant Professor of Medicine, Harvard Medical School
1998-	Assistant Clinical Professor of Medicine, Harvard Medical School

Hospital Appointments:

1974-1975	Assistant Attending in Medicine, Montefiore Hospital, Bronx, NY
1975-1977	Clinical Associate in Medicine, Massachusetts General Hospital, Boston, MA
1977-1978, 1980-1986	Assistant in Medicine, Massachusetts General Hospital, Boston, MA
1987-1992	Assistant Physician, the Medical Service, Massachusetts General Hospital, Boston, MA
1992-	Associate Physician, the Medical Service Massachusetts General Hospital, Boston, MA

Other Professional Positions and Major Visiting Appointments:

1998-	President, Occupational Health Initiatives, Inc.
1998-	President, Occupational Health Institute
1996-1998	Executive Director, Public Health Research Institute
1996-1998	Medical Director & Executive Vice President, Public Health Resource Group, Inc.
1992-1998	Medical Consultant to the Commissioner of the Massachusetts Department of Industrial Accidents on implementation of medical provisions of the Massachusetts Workers Compensation Reform Act of 1991
1989	Adjunct Faculty, Department of Work Environment, University of Massachusetts Lowell
1979	Visiting Lecturer, Harvard School of Public Health
1979-1981	Occupational Physician, Medical Staff, Oil, Chemical and Atomic Workers International Union
1975-1978	Primary Care Physician, MGH Chelsea Health Center
1974-1975	Primary Care Physician, Morrisania Neighborhood Family Care Center, Bronx, NY
1971-1972	Director, Family Planning Clinic, Wake County Health Department, Raleigh, NC

AWARDS and HONORS:

1966	Phi Beta Kappa
1970	Alpha Omega Alpha
2006	Cushing-Gavin Award, The Labor Guild, Archdiocese of Boston

SERVICE ASSIGNMENTS:

1990-1996	Director, Occupational and Environmental Medicine, Massachusetts General Hospital
1990-1993	Assistant Director, MGH Employees Health Service
1980-1990	Co-Director, Occupational Medicine, Massachusetts General Hospital

MAJOR COMMITTEE ASSIGNMENTS:

Harvard School of Public Health:

1980-1983, 1992-	Advisory Committee, Residency Training Program in Occupational Medicine

Hospital:

1989-1990	Subcommittee on Human Studies, Member, Massachusetts General Hospital
1991-1996	Pulmonary and Critical Care Fellowship Review Committee, Member, Massachusetts General Hospital

Regional:

2003-	Contractor to Massachusetts Department of Public Health to consult on development of an asthma education program for construction workers and train community health care professionals to recognize occupational asthma
2001-	Member, Multiple Chemical Sensitivity Advisory Group, Massachusetts Department of Public Health
2000-2001	Member, Institutional Review Board, New England Research Institute, (NERI)
1995-1998	Science Advisory Board, The Massachusetts Toxics Use Reduction Institute, Governor-Appointed Member, the Commonwealth of Massachusetts
1994-	Asthma Treatment Guidelines Subgroup, Health Care Services Board, Chair, Massachusetts Department of Industrial Accidents
1993-1994	Program Committee, Regional Conference on Ergonomics, Safety, and Health in Construction, Member, Massachusetts Construction Safety Congress

1992-1998	Health Care Services Board, Commonwealth of Massachusetts, Chair
1998-	Health Care Services Board, Commonwealth of Massachusetts, Member
1984-1988	Scientific Advisory Council, Center for Health Promotion and Disease Prevention, Massachusetts Department of Public Health, Member

National:

1994	Planning Committee, Hazardous Waste Surveillance Program, Member, National Institute of Occupational Safety and Health/US Department of Energy
1992-1993	Planning Committee, International Congress on the Health Effects of Hazardous Wastes, Member, National Institute Environmental Health Sciences/EPA
1992-1993	Scientific Peer Review Committee for Enhanced Medical Surveillance Program for Beryllium Workers, Member, US Department of Energy
1990	Program Committee, Conference "The Third Wave of Asbestos Disease: Exposure to Asbestos in Place. Public Health Control", Member, Mt. Sinai School of Medicine, New York, NY; Harvard Medical School
1989	Steering Committee, Workshop on Environmental and Occupational Asthma, Member, EPA Task Force on Environmental Cancer and Heart and Lung Disease
1980-1982	Mine Health Research Advisory Committee, Member, National Institute for Occupational Safety and Health

MAJOR ADMINISTRATIVE RESPONSIBILITIES:

1998-	President, Occupational Health Initiatives/Institute
1996-1998	Executive Director, Public Health Research Institute
1996-1998	Medical Director and Executive Vice President, Public Health Resource Group
1992- 2000	Principal Investigator - Research project on health and safety hazards for construction workers on Boston Central Artery/Harbor Tunnel construction project, Public Health Research Institute
1990-1994	Director, MGH Occupational Health Associates, Massachusetts General Hospital

PROFESSIONAL SOCIETY INVOLVEMENT:

1975-	American Public Health Association, Member
1978-	American College of Occupational and Environmental Medicine (ACOEM), Member
1979-	Society for Occupational and Environmental Health, Member, Governing Council, 1986-1989
1982-	Massachusetts Medical Society
1982-1983	Council on Occupational Health, National Association for Public Health Policy, Secretary

1982- American College of Preventive Medicine, Fellow
1983- New England Occupational Medicine Association, Member Board of Directors 1983-1984
1984- American Thoracic Society, Member Program Committee, 1989-1992
1984- International Commission on Occupational Health, Member
1990- Association of Occupational and Environmental Clinics (AOEC), Member
1992- Collegium Ramazzini
1998- Physicians for Social Responsibility, Distinguished Physician

EDITORIAL BOARDS:

1990- American Journal of Industrial Medicine
1995- Applied Occupational and Environmental Hygiene

PART II:

A. Report of Teaching

1. Local Contributions

a. Medical School Courses

- Elective tutorial field study program in occupational medicine with the Oil, Chemical and Atomic Workers International Union
  Organizer and Course Director
  Four to five Harvard medical students; postgraduate students, Harvard School of Public Health; medical residents, Harvard Teacing Hospitals
  - Curriculum in Occupational Medicine funded by the National Fund for Medical Education
  Developer and Codirector, lecturer
- 20 Medical and postgraduate occupational health students: Harvard Medical School, Harvard School of Public Health
- Introduction to Clinical Medicine
  Clinical preceptor; lecturer on Occupational History Taking
  100 Medical students, lecture; three students, clinical preceptorship
- Patient-Doctor III
  Tutor
  Six Medical students
- Pathophysiology, Respiratory
  Lecturer, occupational lung disease; 100 medical students

b. Graduate Medical Courses/Seminars/Invited Teaching Preparations

- Occupational and Environmental Lung Disease
  Lecturer, introductory lecture series for first year pulmonary fellows
  Six to eight postdoctoral pulmonary fellows, MGH/Partners

- MGH Medical Grand Rounds/Malignant Mesothelioma
- MGH Medical Grand Rounds/Occupational Asthma
- Lecturer; MGH medical staff, house officers, fellows
- MGH Women in the Workplace Conference
  Lecturer, Occupational Risk Factors for Women
  Female hospital workers, approximately 50 attendees
- MGH Pulmonary/Critical Care Grand Rounds
  Lecturer, Medical-Legal Aspects of Occupational Medicine
  Lecturer, Occupational Asthma
  Lecturer, Occupational Lung Disease
- MGH Allergy Associates
  Lecturer, Occupational Asthma
  Lecturer, Building-Associated Illness
- Spaulding Rehabilitation Hospital
- Medical Grand Rounds, lecturer - Occupational Medicine

c. Continuing Medical Education Courses

- Massachusetts General Hospital, Harvard Medical School, Harvard School of Public Health: CME Course on Current Concepts in Asbestos-Related Disease
- Harvard Medical School Department of Postgraduate Education on Pulmonary/Critical Care Medicine
  Lecturer, occupational and environmental lung disease
- American Lung Association of Greater Norfolk County
  Lecturer, Occupational Lung Disease: an Overview
- Harvard Medical School Department of Postgraduate Education on Human Teratogens
  Lecturer on associations with occupational and environmental exposures

d. Advisory and Supervisory Responsibilities in Clinical Setting

- Director of elective in Occupational/Environmental Medicine for MGH Allergy/Immunology fellowship program
- Attending on the Pulmonary Consult Service
  Two to four trainees: average of two postdoctoral pulmonary fellows, one medical student
- Supervision of postdoctoral pulmonary fellows in interpretation and signout of pulmonary function tests performed in the MGH Pulmonary Laboratories
  Two to four trainees
- Supervision of postdoctoral pulmonary fellows in ambulatory care setting for patients with occupational/environmental lung disease on an ad hoc basis
  Fifteen trainees

e. Leadership Roles

- Title: (See IID, A1) Courses in occupational/environmental medicine for Harvard

medical students and other postgraduate students and residents
Primary Responsibilities: Development and organization of course curricula, contacting and scheduling lecturers, and preparation and presentation of teaching materials

- Special Accomplishments: 1) introduction of this type of course material (i.e., occupational and environmental medicine) back into the Medical School curriculum; and 2) the organization of courses that provided the opportunity for both didactic, tutorial, and worksite experience for students, as well as introduction to medical-legal and political aspects of occupational medicine, aspects to which students would not have had access otherwise.
- Title: "Asbestos in Commercial Buildings"
  Primary Responsibilities: Conceptualized, organized and moderated an interdisciplinary day-long seminar at the MGH
  Special Accomplishments: Invited lecturers, prepared teaching materials and syllabus, and created forum for discussion among affected parties of the burgeoning public health issue of asbestos in buildings. Attendees included physicians, attorneys, and building owners, developers, and mortgage lenders.

2. Regional, National or International Contributions

a. Invited Presentations

-Speaker and participant. Global Asbestos Congress. Osasco - Sao Paulo, Brazil
- Invited testimony before the House Judiciary Committee of the United States Congress on the HR 1283, the "Fairness in Asbestos Compensation Act of 1999"
- Panelist, "Women's Health Care in the 21st Century", Annual Conference, National Association of Commissions for Women, Boston, MA
- Lecture, "Multiple Chemical Sensitivity": A Wake-Up Call for the Public Health Community
  New England Public Health Association
- Lecture, Multiple Chemical Sensitivity
  Massachusetts Bar Association Environmental Law Committee
- Lecture, Multiple Chemical Sensitivity: Case Studies
  Massachusetts Continuing Legal Education, Inc.
- Lecture, Building-Associated Illness
  Administrative Law Judges Continuing Education, Massachusetts Department of Industrial Accidents
- Medical Grand Rounds, Occupational and Environmental Medicine
  St. Vincent's Hospital, Worcester, MA
- Lecture series for medical house officers; lecture on Occupational Medicine
  New York University (Bellevue) Hospital, New York, NY
- Lecture, Occupational Asthma, Occupational Medicine Residents
  University Hospital, Boston University
- Lecture, Medical Aspects of Workers' Compensation in Massachusetts - Medical and nursing staff

U Mass Worcester Medical Center, Worcester, MA
- Panel discussant, Health Hazards of Asbestos and Other Fibers
The Societe Internationale de Chirurgie, Paris, France-31st Congress
- Lecture, "Environmental Exposures and Risk Management", Environmental Health Education Project for Physicians and Health Professionals, Holyoke, MA
Massachusetts Department of Public Health
- Invited faculty member and lecturer on "Pleural Plaques and Lung Function"
American College of Chest Physicians, 57th Annual Scientific Assembly, San Francisco, CA

b. Professional Leadership Roles Related to Teaching

- EPA, Workshop on Environmental and Occupational Asthma, Task Force on Environmental Cancer and Heart and Lung Disease, Long Beach, CA to develop a teaching program and materials for primary care physicians nationwide
Member Planning Committee; lecturer on "Occupational and Environmental Asthma: Legal and Ethical Aspects of Patient Management"
-American Society for Testing and Materials (ASTM)
Medical Session Chair and lecturer at the ASTM Conference on Indoor Air Quality, Johnson State College, Johnson, VT. ASTM conferences are international conferences held every five years to discuss timely and health-related issues.
-Massachusetts Department of Industrial Accidents, Massachusetts Medical Society
Teaching effort has been the organization and presentation of teaching materials in the area of medical issues in workers' compensation reform, primarily in the area of medical treatment guidelines in workers' compensation in general and treatment guidelines for occupational asthma in particular.
Lectures in this area have included the following: "Workers' Compensation: A Guide for Physicians", "Medical Treatment and Utilization Review. Massachusetts Workers' Compensation in the 1990's: Problems, Procedures and Perspectives", and "Treatment Guidelines and Utilization Review in Workers' Compensation in Massachusetts". Audiences have included members and officers of the Massachusetts Medical Society, the Eastern Association of Workers' Compensation Boards and Commissions, and the Southern Association of Workers Compensation Administrators

c. Professional Leadership Activities

2004: NIOSH Scientific Workshop relating to B Reader Certification Program.
Invited participant
2007: NIOSH Asbestos White Paper entitled "Asbestos and Other Mineral Fibers: A Roadmap for Scientific Research"
Invited Peer Reviewer

B. Clinical Activities

1. Clinical Practice - Field: Occupational/environmental medicine; Areas of major focus: a) occupational asthma; b) airways disease associated with construction work; c) asbestos-related disease; d) chemical sensitivities; and e) building-associated illness. Site of practice: MGH Pulmonary Associates.
2. Time Commitments - 25% Patient care; 5% teaching; 20% administration; 40% consultation; 10 % research.
3. Patient load, complexity - 15% asbestos-related disease; 20% building-associated illness; 20% chemical sensitivities; 35% occupational asthma; and 10% other.
4. Clinical program development - MGH Occupational Health Associates was an attempt to bring together a multidisciplinary team to provide medical services in the area of occupational medicine. Presently Dr. Oliver has one of the largest medical practices in the New England area for patients with building-related illness and chemical sensitivities.

C. Scholarly Contributions-Research that Contributes to the Care of Patients

1. Current Research Projects
   - Research on asthma in heavy and highway construction workers.
   - Research on asbestos-related in public school custodians, a 12 year longitudinal follow-up study.

2. Research Funding Information
   - Current years covered October, 2002-March, 2003; funding source Center to Protect Workers' Rights/NIOSH; Principal Investigator; "Asthma in Heavy and Highway Construction Workers Exposed to Silica".
   - Current years covered 1999-2003; funding source Manville Property Damages Trust; Principal Investigator; "Asbestos-Related Disease in Public School Custodians: a Longitudinal Follow-Up Study".

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UNITED STATES DISTRICT COURT
FOR THE
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY; And As ADMINISTRATRIX OF THE ESTATE OF DANIEL ALLEN; And AS NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; And MARK ALLEN, Plaintiffs; v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES; And SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION No.: 05-40048

RULE 26 EXPERT REPORT- L. CHRISTINE OLIVER, M.D.

I am writing with regard to the results of my medical evaluation of Coach Daniel Allen. My findings and opinions, and the bases for these opinions, are provided below. These are based upon my review of the following: 1) medical records; 2) a personal exposure and symptom diary kept by Mr. Allen; 3) Southwest Recreational Industries, Inc.'s Supplemental Responses to the Plaintiffs' Request for the Production of Documents; 4) Material Safety Data Sheets (MSDS) for products used during the installation of Versaturf '360' in the Field House of The College of the Holy Cross in Worcester, MA in late May/early June, 2001; 5) the Technician's Manual for the Installation of Versaturf '360'; 6) email correspondence between Mr. Allen and administrative personnel at Holy Cross College; 7) affidavits of co-workers of Mr. Allen and of one of the applicators of the Versaturf flooring system; 9) deposition testimony of a) Rod Paul, an employee and Projects Manager at Southwest Recreational Industries at the time of the installation of the floor, b) Scott Merrill, Director and former Assistant Director of the Physical Plant at Holy Cross College, and c) Mrs. Laura Allen, Mr. Allen's widow; 10) expert report; 11) observations at the time of a walk-through inspection of the Field House at Holy Cross College, including the gymnasium itself and the office of Coach Allen; and 12) floor and heating, ventilation, and air conditioning system (HVAC) plans for the Field House.

Medical records are from the UMass Memorial Medical Center (UMMC) in Worcester, MA and the offices of Drs. Richard A. Palken, Daniel A. Pollen, David A. Chad, Nicholas Smyrnios, Stephen J. Krinzman, Brian D. Busconi, and John V. Shufflebarger of UMMC; James A. Russell, DO of the Lahey Clinic in Burlington, MA; Harvard Pilgrim Health Care; and Sharon Home Health Care. Medical records cover the time period October 3, 1992 through May 11, 2004. Dated email and written correspondence cover the time period August 2, 2002 to August 12, 2003. Co-workers from whom affidavits were obtained are Robert J. Bradley, Paul T. Bachia, and Larry Napolitano; the Versaturf '360' applicator is Paul Crecelius. Affidavits were signed on May 18, May 19, May 10, and May 11 2007, respectively. Deposition testimony was taken of Mrs. Allen on March 13, 2007 in Boston, MA; of Mr. Paul, on April 11, 2007 in Baltimore, MD; and of Mr. Merrill, on June 14, 2007 in Boston. Expert report is from Marcia H. Ratner, PhD, Director and Neurologist and Neurotoxicologist, respectively, of the Environmental and Occupational Neurology Program and Department of Neurology at Boston University School of Medicine, dated June 14, 2007.

In addition, I have relied upon my own professional experience and publications in the medical and scientific literature. These include but are not limited to those provided at the end of this report. A copy of my current curriculum vitae has been provided.

I anticipate the review of an expert report by William Ewing, CIH, of Compass Environmental in Marietta, GA when it becomes available.

Medical History

Mr. Allen was in his usual state of good health until May, 2001. On or about May 22 of that year, the process of installing the Versaturf '360' polyurethane flooring system in the Field House at Holy Cross College was begun. Early in the course of the installation Mr. Allen, as described in his diary, was "overcome with the fumes" and "developed a severe headache, nausea with dizziness as well as disorientation." As the day went on, his symptoms became worse to the point that the room was spinning and he had to leave. The following day he returned to work, only to find that the fumes had not dissipated. Headache and nausea persisted.

Mr. Allen vacationed with his wife in Aruba from July 23-29. While on vacation he developed "severe diarrhea", treated with Ciprofloxacin. On August 3, 2001 he was seen by Dr. Palken, his primary care physician. The office note indicates diarrhea for eight days, and headache, dizziness, and "sweaty." On August 29, September 18, October 22, and October 23 Mr. Allen was seen by Dr. Palken or contacted his office because of persistent headache, dizziness, and nausea. On October 23, Dr. Palken notes headache, increasing in severity and frequency. He ordered a brain MRI/MRA and prescribed Neurontin. MRI/MRA on October 30 was within normal limits.

On November 15, 2001 Mr. Allen was evaluated by Dr. Pollen in the Headache Clinic of UMMC. A history was obtained of throbbing bilateral temporal or occipital

headaches that worsened during the course of the day and had been associated with vertigo and nausea for the three weeks preceding the visit. On an intake form completed by Mr. Allen at the time of that visit he noted both nocturnal and daytime calf cramps and muscle twitching. Neurologic examination by Dr. Pollen was normal. He concluded that Mr. Allen had headaches of "transform migraine", with related vertigo, as well as "restless leg syndrome." Neurontin was continued and the dose increased.

Mr. Allen notes in his diary that in September he developed muscle fasciculations as well, in his legs. He also notes at that time that "I did not mention anything to my doctor about the exposure because I didn't put it together that that was what caused my condition." In October headaches and dizziness persisted and at times made it difficult for him to function. During the fall of 2001 fasciculations in his lower extremities increased and spread to his arms and upper body. In his diary he writes "I basically dealt with it for a couple of more months."

Dr. Palken referred Mr. Allen to Dr. Chad, neurologist at UMMC, for evaluation of fasciculations. Mr. Allen obtained an earlier appointment with Dr. Russell, neurologist at the Lahey Clinic, and was seen by him on January 22, 2002. At that time, Mr. Allen was noted to be a 46 year old left-handed football coach at Holy Cross referred for assessment of fasciculations, with elevated creatine phosphokinase (CPK) at 511. History revealed onset of fasciculations in the thigh and right shoulder in approximately August, 2001. He also reported fatigue but denied functional impairment. There was no history of weight loss or symptoms of autonomic nervous system dysfunction. There was also no family history of motor neuron disease (MND). Medications were Zestril for hypertension, neurontin for headache, and aspirin for cardiovascular prophylaxis. Physical examination revealed diffuse fasciculations over the shoulders and thighs, primarily. Mr. Allen appeared anxious and blood pressure was elevated at 140/100. Left foot dorsiflexion was intact but dorsiflexion of the left great toe was markedly diminished at 4- (vs. 4+ on the right). Deep tendon reflexes were decreased in the right upper extremity compared to the left. Mr. Allen was unable to walk on his left heel. He was able to do single leg-toe rises bilaterally, better on the right than the left. Pin prick and vibration were decreased over the left great toe compared to the right. Grip strength was 104 lbs on the right and 127 lbs on the left. Dr. Russell's initial assessment was that Mr. Allen's presentation with fasciculations was unusual for MND; however, the widespread nature of the fasciculations, taken together with left foot drop and elevated CPK, were considered indicative of a pathologic process. Dr. Russell ordered nerve conduction and electromyographic (EMG) studies. The former were within normal limits. The latter showed "widespread fasciculations and findings of chronic denervation and reinervation."

On January 28, 2002 Mr. Allen was examined by Dr. Chad at UMMC. He reported to Dr. Chad the resurfacing of the floor of the Field House and the symptoms he experienced during that time. Physical examination by Dr. Chad revealed multisegmental fasciculations involving the muscles of the upper back, shoulder, upper arm, forearm, and thighs. No muscle atrophy was appreciated. Weakness of the left foot and toe extensors was described. Right biceps and brachioradialis reflexes were decreased and "brisk" for right triceps and leg reflexes. Heel walking was abnormal because of weakness of the left

foot. The remainder of the neurologic exam was normal. It was Dr. Chad's opinion that symptoms, physical findings and EMG results suggested MND. Lyme titer and 24-hour urine for heavy metals were ordered. Mr. Allen was given a prescription for Rilutek and advised to take vitamins C and E. Lumbar puncture was attempted on the following day without success and performed under fluoroscopic guidance on February 15. The cerebrospinal fluid (CSF) was clear, with normal protein, glucose, and cell count, and negative VDRL.

Mr. Allen was seen in follow-up by Dr. Russell on February 18, 2002. At that time he appeared healthy and had noted no change in symptoms. There was no evidence of bulbar involvement. Right grip strength was increased 12 lbs compared to January; and left grip, decreased by 1 lb. Lower extremity strength was normal, as was walking. It was Dr. Russell's conclusion that Mr. Allen had probable MND. He so counseled the Allen family. He prescribed quinine sulfate for muscle cramps and raised the question of Mr. Allen's participation in a study investigating the therapeutic utility of Celebrex. On February 22 Dr. Russell noted that the following test results were normal: Lyme screen; MRI of the cervical spine; 24-hour urine for arsenic, lead, and mercury; CBC; erythrocyte sedimentation rate; serum protein electrophoresis; CSF antiglycolipid antibody (GM1); and B12. Thyroid stimulating hormone was mildly elevated at 4.4.

In early March, 2002 Dr. Palken diagnosed reactive depression and prescribed Remeron. When next seen on August 2, Mr. Allen reported persistent "cramps" and a history of having received intravenous EDTA. Physical exam revealed "palpable and visible fasciculations" and lower extremity weakness of the dorsiflexor muscles. He noted that Mr. Allen could not walk on his heels and could barely walk on his toes. Bilateral clonus was noted. His assessment was amyotrophic lateral sclerosis (ALS). When next seen by Dr. Palken on October 2, 2002 Mr. Allen reported a tickle in his throat and dizziness and nausea when at work in the Field House, but not outside of the Field House. His legs were weak, the left greater than the right. He reported no upper body weakness. Medications were Synthroid, folic acid, calcium and magnesium, and vitamins E and C. Chest X-ray on that day was reportedly normal. Spirometry performed on October 4 was normal: FEV_1 (L) 4.54, 121% predicted; FVC (L) 4.99, 99% predicted; FEV_1/FVC 0.91; PEF (L/sec) 9.63, 104% predicted.

In the spring of 2003, Mr. Allen became wheelchair-bound because of inability to walk. In late December he was referred by Dr. Palken to Dr. Smyrnios of the UMMC Division of Pulmonary, Allergy, and Critical Care Medicine because of dyspnea. The dyspnea was noted by Dr. Smyrnios to be "manifested primarily by inability to generate an adequate voice because he does not get enough air." He further noted that Mr. Allen was able to stand with partial support for only three to four minutes. He was also unable to use his arms and had not been able to write since June. There was no history of prior respiratory tract illness or disease, and no history of tobacco use. He was able to eat, with occasional cough. Medications were amitriptyline, Klonopin, Benzphetamine, vitamins E and C, repoic acid, folic acid, and Probiotics. Physical examination revealed Mr. Allen to be "thin and debilitated", seated in a wheelchair. Tongue movements were normal and

there were no fasciculations. Lungs were clear. Fingers were contracted and he was not able to move his arms or legs. Pulse oximetry was normal at 98%.

On January 4, 2004 Mr. Allen was seen in follow-up by Dr. Smyrnios and lung function tests were obtained. Spirometry showed marked decreased in FEV_1 and FVC compared to October, 2002: FEV_1 (L) 1.18, 32% predicted; FVC (L) 1.40, 28% predicted; FEV_1/FVC 0.84. Total lung capacity was reduced at 50% predicted; single breath diffusing capacity for carbon monoxide (DLCO) was normal with correction for alveolar volume at 128% predicted. Maximal inspiratory and expiratory muscle forces were markedly reduced at 27 and 28 cm H_2O, respectively. Chest radiograph showed low lung volumes. Dr. Smyrnios concluded that Mr. Allen had neuromuscular disease consistent with ALS from a pulmonary standpoint. He noted "dramatic deterioration over the past 14 months", with respiratory failure being an imminent threat. Dr. Smyrnios prescribed BiPAP and cough in-exsufflator to assist Mr. Allen breathing. At that time Mr. Allen declined a feeding tube. Tracheotomy and mechanical ventilation were also discussed.

On April 13, 2004 Mr. Allen was examined by Dr. Joe Jabre and Marcia Ratner, PhD at the Boston University School of Medicine. Neurologic exam revealed generalized weakness of his upper and lower extremities to the point of his being wheelchair-bound, contractures of his hands and feet, atrophy and fasciculations of his tongue, absent deep tendon reflexes at the ankle and knee, positive Hoffman's, and mild loss of pinprick sensation in his lower extremities.

One week later on April 21 Mr. Allen was seen in follow-up by Dr. Smyrnios. By that time, Mr. Allen had developed trouble swallowing and eating and drinking. He was able to take only a few sips of liquid at a time. BiPAP was used only intermittently because the air was dry and the machine uncomfortable. Secretions were increased and the cough in-exsufflator ineffective in removing them from the chest. Physical exam revealed him to be in a wheelchair, frail-appearing and speaking in a soft voice. He had tachycardia attributed to dehydration. Dr. Smyrnios' assessment was ALS, rapidly deteriorating and without benefit from homeopathic remedies. In his opinion, a feeding tube was needed. He prescribed intravenous hydration at home and nasal pillows and humidification for the BiPAP machine. Sharon Home Health Care saw Mr. Allen on the same day. On May 4, 2004 Mr. Allen was admitted to UMMC for hydration and placement of a gastric feeding tube (PEG). Arterial blood gases on admission were consistent with respiratory failure: pH 7.36, pO_2 68 mmHg, pCO_2 71 mmHg. PEG placement was performed at the bedside, as the family did not want Mr. Allen intubated and placed on a ventilator.

Mr. Allen was discharged in stable condition on May 7, 2004 to be followed at home by the Visiting Nurse Association, with additional care from home health aides. He died nine days later on May 16. Records of the events immediately surrounding his death are not available. The death certificate gives as cause of death "neuromuscular degeneration." Postmortem examination was not performed.

Past medical history reveals hypertension and bifrontal headaches. In 1992 he tore his rotator cuff on the left, with subsequent acromioclavicular joint arthritis and mild

impingement. He was followed for this problem by Dr. Busconi, and in 2000 had arthroscopy with debridement and subacromial decompression. Other surgical procedures included appendectomy, hand surgery, hernia repair, and vasectomy. On May 3, 2001 he underwent colonoscopy because of blood in his stool; findings were normal and blood was attributed to daily aspirin. On May 14, 2001 he underwent removal of skin tags on his back and a sebaceous cyst on his scalp. On May 22, 2001 he was seen by a nutritionist with regard to implementation of a weight loss regimen. Mr. Allen was active throughout his adult life. He did not use tobacco; alcohol consumption was limited to a couple of beers per week. His only known drug allergy was to Paxil. Family history reveals that his mother smoked cigarettes and died of lung cancer at age 58 or 59. Mr. Allen never knew his father. Mrs. Allen testified (p.19) that to her knowledge his father lived to at least 80 years of age, with diabetes mellitus being his only known disease. He had one brother, in good health with high blood pressure. One half-brother and four half-sisters were alive and well in 2004, with the exception of hypertension. Mr. Allen has three children, ages 19, 14, and 12 at the time of his death. One of his children has Hashimoto's thyroiditis. At the time of his death, Mr. And Mrs. Allen had been married for 27 years. She is a registered nurse.

Occupational and Exposure History

Occupational history reveals that Mr. Allen graduated from Purcell High School in Cincinnati, OH in 1974. He attended Hanover College in Indiana and then obtained a Master's degree in school administration from the University of Dayton. He worked as a graduate assistant to the football team there for one year after graduation and then took a job at Mariemont High School in Cincinnati. He taught science and coached football and track from approximately 1979 to 1981. From 1981 to 1982 he worked as assistant football coach at Hanover College. In 1982 Mr. Allen went to work for The College of the Holy Cross as assistant football coach. He held this position until 1990 when he went to work for Boston University as head coach for the football team. In 1995 when Boston University abolished their football program, he went back to Holy Cross as head football coach. He held this position until November, 2003 when he was terminated because of his MND and its attendant disability.

Southwest Recreational Industries, Inc.'s Responses to the Plaintiffs' Request for the Production of Documents reveal that in the spring of 2001 The College of the Holy Cross contracted with Southwest Recreational Industries (D/B/A Martin Surfacing) to resurface the flooring in the Field House during the time period May 21 to June 8, 2001. According to the terms of the agreement, 17,000 sq.ft. of flooring was to be resurfaced with Versaturf '360' – a 100% mercury-free polyurethane athletic surface. The installation included gamelines and coatings as they presently existed.

Specifications for projects such as the one carried out in the Field House at Holy Cross College call for the removal and disposal of the top 1/16 inch of floor surface, to be replaced by a 1/8 inch Versaturf '360'surface. According to testimony by Rod Paul, the installation process calls for the deep cleaning or abraiding of the existing surface with a drum sander. Then a primer is spray-applied for adhesion. After the primer has dried, the

polyurethane floor is poured. The polyurethane is prepared by machine-mixing Parts A and B and transferring them by a hose into 5-gallon buckets. It is poured from the buckets over the entire floor, raked out, and allowed to dry. Finally a coating is sprayed on and the gamelines painted. The drying of both primer and polyurethane are affected by heat and humidity – with higher temperature and relative humidity retarding drying. Mr. Paul testified (pp.32, 33) that to keep humidity at the proper level "…. if you haven't already done so, to make sure that the … either the heat or the air conditioning is on in the building to reduce the relative humidity." The Technician's Manual for the Installation of Versaturf '360' specifies (Section 8, 4) that the technician should (a) "make sure the HVAC system is operational and running before you begin" and (b) "if it is on a timer, it should be by-passed to keep the heat or AC running." Section 24 states "Each time you run the machine, it must be flushed with trichloroethane immediately after."

Mr. Merrill testified that an HVAC system installed in the Field House in approximately 1992 as part of a larger renovation project serviced the Athletic Department offices on the first and second floors of the Field House, but not the gymnasium itself (pp.26, 27; lines 4-15 and 14-21, respectively). He also testified (p.83, lines 4-8) that the air in the gymnasium is "not conditioned air", i.e., it is neither heated nor cooled/dehumidified.

Specifically with regard to the installation of Versaturf '360', Mr. Crecelius described the following: 1) sanding the existing floor with a Ryder Sander to "rough up" the floor, 2) cleaning and vacuuming the floor, 3) spraying the floor with a primer, 4) applying a resin coating approximately 1/8 inch thick to the floor, 5) spray painting the floor to the desired color, and 6) laying out the gamelines and painting them by roller. He noted that the applicators wore a "full-face organic filter respirator" during the process. Mr. Crecelius described taping the doors leading into the lobby area with plastic and using a large industrial fan to blow the fumes out of the work area after the floor was dry. He indicated in his affidavit that "If the field house had air conditioning and/or heat, it would not be turned on" while the floor was drying.

Part G of the Responses to the Plaintiffs' Request was "The Material Safety Data Sheet (MSDS) for each product used for the Project." Part G consists of MSDSs for the following products: Versaturf '360' Part A, manufactured by Southwest Recreational Industries (MSDS dated April 14, 1999); Mondur 448 Part B, manufactured by Bayer Corporation (MSDS dated January 1, 1996); Richmold 303-0002, manufactured by Carpenter Company Chemical Systems Division (MSDS dated October 29, 1997); Futura Tech 506A Clear 1:1, manufactured by Futura Coatings, Inc. (MSDS dated February 4, 1997); Futura Tech 506B 1:1 (MSDS dated February 4, 1997); D-186 Primer, manufactured by Development Associates, Inc. (MSDS dated December 12, 1994); Futura Tech 8553B, manufactured by Futura Coatings, Inc. (MSDS dated February 12, 1997); Futura Tech 8553A and 8563A (MSDSs dated December 12, 1996); and Futura Tech 8563B Red Line Paint (MSDS dated October 27, 1997).

Solvents contained in these products include polyoxy propyleneglycol 65% by weight (Versaturf '360'); aromatic hydrocarbon NOS 45-61%, acetone solvent 0-14% (Futura Tech 506A Clear); toluene 5-20%, ethanol 40-70%, 2-ethylhexanol 1-10%, and diacetone alcohol 1-10% (D-186 Primer); aromatic hydrocarbon NOS 10-26%, glycol ether acetate 10-26% (Futura Tach 8553B All Colors); and aromatic hydrocarbon NOS 27-43% (Futura Tech 8553A). Trichloroethane was used to clean the machines after each application. Versaturf '360' also contained methlene bis (phenylisocyanate) (MDI); and Mondur 448, higher oligomers of MDI and 2,2, 2,4, and 4,4 diphenylmethane diisocyanate.

In his diary, Mr. Allen described being "overcome" with fumes during the installation of Versaturf '360' in the Field House. He further described persistence of fumes during the period of the resurfacing. Mr. Robert (Bob) Bradley was Assistant Football Coach in the spring and summer of 2001. He testified in his affidavit that his office was about ten yards from Coach Allen's office, on the same floor. He estimated that the resurfacing was carried out about ten yards below his and Coach Allen's offices. He recalled that the weather during the period of the floor installation was hot and humid and that the air conditioning was on; so that the windows would have been closed. Mr. Bradley testified that "During the re-surfacing work, I smelled and felt the effect of the fumes from the chemicals being used by the workers; the fumes were noxious; I felt dizzy and suffered headaches throughout this period." He noted that before the resurfacing began "Coach Allen appeared perfectly healthy to me." At the time, the football coaches and their staff were preparing for the annual Football Camp, scheduled to begin just after completion of the floor installation. Coach Allen let his staff and assistants leave early each day because of the chemical exposures; but he stayed to finish preparations for the Camp.

Mr. Paul Bachia was the Running Backs Coach at this time. He testified in his affidavit that his office was directly across from Coach Allen's office. He concurred with Mr. Bradley that the resurfacing was carried out about ten yards below the offices on the second floor. As he recalled, the work took approximately two weeks. Mr. Bachia describes smelling and feeling "the effect of the fumes from the chemicals being used by the workers: I felt a burning sensation in my eyes and, when I breathed deeply, I felt a burning sensation in my throat." He also described feeling lightheaded and noted that Coach Allen was lightheaded and nauseous. Mr. Napolitano was the coordinator of athletic media relations at Holy Cross College in May, 2001. His office was on the ground floor of the Field House. He testified in his affidavit that the workers were "right outside my office door at one point. They were directly underneath Coach Allen's office." He reported pounding headaches and nausea during the period of the resurfacing. Headaches were directly linked to his presence in the Field House. He noted "The smell just permeated everything and with the heat rising to the top of the building it was just worse and worse every day. I could tell it was worse where Coach Allen was located, when I would go up and see him. At least I could open my windows to the outside. He could not open his windows."

According to Mr. Merrill's testimony (p.76, lines 9-11), air quality testing was carried out in the gymnasium on August 15, 2002, over a year after the installation of the

flooring system. An email from Mr. William Conley to Mr. Allen dated September 20, 2002 reports the results of air quality testing done in the Field House. Mr. Merrill's testimony (p.76, lines 9-11) indicates that the testing was carried out on August 15, 2002. Results as described in the email revealed elevated levels of volatile organic compounds (VOCs), attributed by Mr. Conley to recent painting in the building, with propylene glycol and methyl ether acetate being the predominant chemicals identified. Also noted were "very high" levels of airborne particulates $\geq$ 0.3 microns in diameter. Levels of MDI were detectable, although in concentrations less than 0.001 parts per million (ppm). The scope and actual results of the air quality testing are not available.

Assessment

In summary, Mr. Allen had a history of occupational exposure to solvent vapors and aerosols at the time of the resurfacing of the gymnasium floor in the Field House at The College of the Holy Cross in Worcester, MA. The exposure occurred in late May/early June, 2001. At the time he was working as Head Football Coach at the College, a position he had held since 1995. His office was on the second floor of the Field House, about 10 yards from the gymnasium. The resurfacing took approximately seven to ten days; although the actual duration of the project is not specified in any of the materials available for review. Mr. Allen estimated a period closer to 14 to 21 days; Mr. Bradley, about two weeks.

In his personal diary, Mr. Allen described being "overcome with the fumes" from the floor resurfacing. Symptoms included headache, dizziness, nausea, and disorientation. Despite these symptoms, he returned to work on a daily basis during this time, as he was preparing for the College's annual football camp. Co-workers in offices proximate to Mr. Allen's reported similar symptoms – headache, dizziness, lightheadedness. When he returned from a July vacation, Mr. Allen's symptoms returned and persisted. In September he developed, in addition, fasciculations in his lower extremities. Subsequently fasciculations spread to his upper extremities and trunk. In October headache increased in frequency and severity.

In January, 2002 Mr. Allen was evaluated by two neurologists – Dr. Chad at UMMC and Dr. Russell at the Lahey Clinic. Based on medical history and physical and laboratory findings, both diagnosed ALS. Mr. Allen's course was relentlessly progressive and he died of his disease on May 16, 2004, approximately 16 months after diagnosis.

In my opinion, Mr. Allen had ALS and died as a result of his disease. Mr. Allen was diagnosed with ALS by his treating physicians in January/February, 2002. Medical records and death certificate indicate that he died less than two years later as a consequence of his disease.

ALS is a degenerative disease of the nervous system affecting the motor neurons, hence its classification as a MND.[1] Males are more commonly affected than females. Age at onset is generally greater than 50 years; incidence increases with increasing age. Approximately 5% are familial, inherited as an autosomal dominant trait. The remainder

are classified as "sporadic", without clearly demonstrated cause. Presenting symptoms are variable and include fasciculations of the upper and/or lower extremities, weakness of the leg and foot drop, and loss of fine finger movements. As the disease progresses, the trunk and respiratory muscles are affected, as are the muscles of the tongue, pharynx, and larynx. Approximately 50% of those affected die within three years; 90%, within six years.

Pathologic examination of the spinal cord and lower brain stem reveals loss of motor neurons in ALS. In some familial cases, mutation of a gene that codes for Cu-Zn superoxide dismutase (SOD) has been described. The result is a 20 to 50 percent decrease in SOD enzyme activity, causing an excess of free radicals that is associated with degeneration of neurons. Additionally, SOD enzyme deficiency is thought to be associated with increase in glutamate concentrations in the extracellular space, with resulting increase in glutaminergic excitotoxicity and motor neuron degeneration. Additional enzymatic and biochemical mechanisms have been proposed as pathogenic in ALS; these are described in detail by Dr. Ratner.[2]

In Mr. Allen's case, initial symptoms were fasciculations in the leg with weakness and foot drop. Symptoms spread to his arms and upper trunk. He developed decrease in respiratory muscle force as a result of muscle weakness, causing severe impairment in lung function. Ultimately muscles of his pharynx and tongue were affected, resulting in difficulty ingesting food and liquid.

In my opinion, Mr. Allen had sporadic ALS. History taken of Mr. Allen himself as reflected in the medical record and deposition testimony of his widow reveal no family history of ALS. As the disease is inherited as an autosomal dominant trait, the absence of family history makes familial ALS most unlikely.

In my opinion, the time of onset and rate of progression of ALS in Mr. Allen's case were causally related to his exposure to solvent vapors and aerosols during the course of the installation of the Versaturf '360' flooring system in the Field House of The College of the Holy Cross.

In late May/early June, 2001 Mr. Allen was working in his office on the second floor at the west end of the Field House. He reported in his diary that he "became overcome with the fumes." At the time, the installation of the Versaturf '360' in the gymnasium had begun. Solvents found in the chemical products used in the installation included toluene, aromatic hydrocarbons not specifically identified because of trade secret, ethanol, 2-ethylhexanol, diacetone alcohol, acetone, glycol ether acetate, and trichloroethane. The primer and coatings were spray-applied, creating an aerosol and enhancing availability for inhalation. Solvent vapors were released into the air from the primer, the polyurethane flooring system, and the coatings as each dried.

The symptoms which Mr. Allen and his colleagues developed during this time period are consistent with neurotoxic effects of solvents – namely headache, dizziness, nausea, and disorientation.[3,4] The occurrence of these symptoms and their persistence suggest that exposures were at or above the permissible exposure limit (PEL) established by the

Occupational Safety and Health Administration (OSHA) of 200 ppm, established as an eight hour time-weighted average for workers in an industrial setting.[5] Exposure of human subjects to toluene at 600 ppm for eight hours has been associated with headache, dizziness, nausea, dilated pupils, and euphoria; symptoms were enhanced with exposure at 800 ppm.[4] Thus, the nature of Mr. Allen's symptoms and the distinct temporal relationship between their onset and persistence and the installation of the Versaturf '360' flooring system are consistent with and make likely a causal association.

These are two of the cornerstones to the determination of exposure-related disease in occupational medicine: consistency of symptoms and clinical manifestations with what would be expected to occur in association with a given exposure and a temporal association between onset/worsening of symptoms and that exposure. Another cornerstone is the use of differential diagnosis to exclude other possible causes. The application of the differential diagnostic method to the review of Mr. Allen's medical records, Mrs. Allen's deposition testimony, and the affidavits of co-workers who knew Mr. Allen well reveals that he was active and healthy prior to the exposures incurred in the early summer of 2001. There is no family history of ALS; so that he did not have familial ALS. Other putative causes include exposure to pesticides and "agricultural chemicals" (which contain solvents), sixty hertz magnetic fields, and welding fume.[6,7] There is no evidence that Mr. Allen had exposure to these agents.

Dr. Ratner in her report has provided ample evidence of the motor neuron toxicity of solvents generally and toluene specifically, with an emphasis on enzymatic and biochemical mechanisms.[2] She has concluded "with a reasonable degree of medical certainty" that Mr. Allen's exposure to the chemicals used in the resurfacing of the Field House gymnasium floor hastened the onset of Mr. Allen's ALS and his consequent demise.

Epidemiologic evidence also supports a causal association between exposure to solvents and the development of ALS. Solvents are well known toxicants for the central nervous system and the peripheral nervous system.[8] Hawkes et al in 1989 was one of the first to raise the question of a causal relationship between occupational exposure to solvents and MND, having observed that of 164 deaths among leather industry workers, 33 (20.12%) were due to MND.[9] The authors suggest that "a direct neurotoxic action effect" of solvents on the motor neurons "deserves most consideration" (p.75). Shortly after the publication of the article by Hawkes, Chio et al in a Letter to the Editor presented data on occurrence of MND among workers in a variety of trades exposed to solvents and glues.[10] These included typesetters, painters, carpenters, tanners, and workers in the rubber production industry. Although failing to achieve statistical significance because of small numbers, for each odds ratios were greater than 1 at 2.4, 2.8, 5.1, 3.7, and 1.7, respectively.

In a case-control study of 103 patients with MND in Scotland, and 103 referents from the community matched on age and gender, Chancellor et al observed a significant increase in risk for exposure to solvents/chemicals among cases compared to the reference group (OR = 3.3, 95% confidence interval (CI) 1.3-10).[11] A case-control study carried out in the northwest region of England examined risk factors for MND, matching each of 128 cases

with two controls based on gender, age, and geographic area of residence.[12] Exposure to fumes and dust was significantly associated with MND (RR = 2.46, 95% CI 1.47-4.09).

Comparing 174 newly diagnosed cases of ALS with 348 matched controls, McGuire et al observed a two fold increase in risk with occupational exposure to alcohols or ketones (OR = 2.0, 95% CI 1.0-4.0) and a 90% increase in risk with exposure to cleaning solvents or degreasers (OR = 1.9, 95% CI 1.1-3.3).[6] For alcohols and ketones, risk was greater in men than in women (OR = 2.6, 95% CI 1.1-6.1 vs. OR = 1.2, 95% CI 0.4-3.7). Exposure was assessed on the basis of job history by a panel of four industrial hygienists blinded as to disease status and self-reported exposures.

Using death certificate data from the National Occupational Mortality Surveillance System, Park et al calculated mortality odds ratios (MOR) for several neurodegenerative diseases, including MND.[7] Usual occupation and business or industry were obtained from the death certificates. Comparison group consisted of all deaths without mention of neurologic disease on the death certificate. Exposure to solvents and benzene was assessed using a standardized job-exposure matrix, with further classification of probability and intensity of exposure: none, low, medium, high. The total number of deaths was 2,614,346; 112,805 were due to neurodegenerative disease. Of these, 6,347 were attributable to MND. A significant elevation of MOR for MND was observed for occupational exposure to solvents (MOR = 1.16, 95% CI 1.01-1.34). Risk factors for sporadic ALS (SALS) were examined in a case-control study in Australia, comparing 179 ALS patients with controls without known neurologic disease.[13] Exposures were self-reported using a structured questionnaire. Significant associations were observed for occupational exposure to solvents/chemicals for the total group (OR = 1.92, 95% CI 1.26-2.93, p=0.003) and for males (OR = 1.85, 95% CI 1.12-3.04, p=0.023) and females (OR = 2.57, 95% CI 1.05-6.31, p=0.066) independently. The authors concluded "that occupational exposure to solvents/chemicals is an important risk factor for SALS in the Australian population."

In a prospective population-based study, Chio et al examined the predictive value of age at onset and symptom progression for survival time in ALS.[14] The cohort consisted of 221 patients with ALS enrolled in the study in 1995 and 1996 and monitored for a little more than five years using a standardized evaluation form. The median age at onset was 62.8 years (standard deviation (SD) 11.2 yrs). The median survival time from age at onset was 915 days (95% CI 790-1065). Age at onset was significantly associated with survival time (p=0.007). Age was noted to be "probably the most consistent factor related to outcome" (p.101), with older age at onset being associated with more rapid progression. Each of the six patients with symptom onset at less than 40 years of age was alive at the end of the follow-up period. Three and five-year survival from age at onset for the group as a whole was 40.5% (SE = 3.5%) and 24.7% (SE = 3.1%, respectively. Mr. Allen was 45 years of age at the time of onset of his disease. His subsequent survival time was approximately 2.7 years.

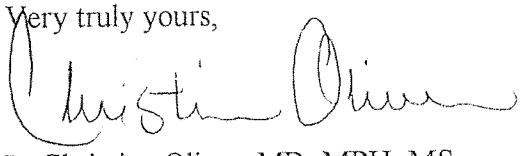
Thus in vitro data from toxicological studies, in vivo data from animal studies, and epidemiologic data from studies in human populations in a number of different countries

all support a causal association between solvent exposure and the development and/or exacerbation of MND in the form of sporadic ALS.

In my opinion, Southwest Recreational Industries, Inc., d/b/a Martin Surfacing, was negligent a) in its failure to warn Mr. Allen and other athletic staff of the potential toxicity of the chemicals used in the installation of the Versaturf '360' polyurethane flooring system and b) in its failure to ensure that these personnel were either adequately protected or vacated from the Field House during the installation process. This opinion is based upon information contained in Mr. Allen's diary and the affidavits of three colleagues working in the building at the time, as well as the known toxicity of the chemicals used in the floor resurfacing. Chemicals contained in the products used include not only solvents with known neurotoxicity, hepatotoxicity, and renal toxicity, but also diisocyanates with well-documented and potentially fatal respiratory toxicity as a result of irritant and sensitizing properties.[15]

I hold all of the opinions expressed in this report to a reasonable degree of medical certainty. I reserve the right to further supplement this report and respond to the reports submitted by the defense.

Very truly yours,



L. Christine Oliver, MD, MPH, MS

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Education

B.S., Biology, Washington and Lee University	1978
Courses in Management, Statistics, Technology and Science Policy (University of Michigan, Georgia State, Georgia Tech)	1978-1988
Short courses in industrial hygiene, toxicology, indoor air quality environmental site assessments, asbestos evaluation and control	1978-Present

Employment History

Compass Environmental, Inc. Technical Director	1993-Present
Diagnostic Engineering Inc. Regional Technical Director	1990-1993
The Environmental Management Group, Inc. Executive Vice President	1987-1990
Georgia Tech Research Institute Research Associate II	1981-1987
Clayton Environmental Consultants, Inc. Industrial Hygienist	1978-1981

Experience Summary

Mr. Ewing is the Technical Director for Compass Environmental, Inc. In this capacity he serves as project manager for industrial hygiene and indoor air quality studies and assessments. His technical responsibilities include project design, execution and report development for private and government project sponsors. He is also responsible for research studies, preparation of papers and publications, and quality assurance. He was the Executive Vice President of The Environmental Management Group, Inc. (TEMG) prior to its acquisition by Diagnostic Engineering Inc. (DEI), where he served as Regional Technical Director. While at the Georgia Tech Research Institute (GTRI) he started the industrial hygiene laboratory, instituted the hazardous waste program for small business in Georgia, and served as an industrial hygienist under the 7(c)(1) program, sponsored by the Occupational Safety and Health Administration (OSHA). As Director of the Asbestos Programs Group, he conducted training, technical assistance, and research on asbestos in buildings, under the sponsorship of the U.S. Environmental Protection Agency (USEPA).

During the past 25 years Mr. Ewing has conducted numerous industrial hygiene, asbestos management, and indoor air quality studies. In the field of industrial hygiene he has conducted over 300 field investigations including textile mills, foundries, steel mills, health care facilities, chemical plants, and manufacturing operations. Among the indoor air quality projects, his experience includes office settings, hospitals, and studies involving off-gassing of volatile compounds from products. He has served as a consultant to the Centers for Disease Control (CDC) on airborne microbial contamination, and is currently an industrial hygiene consultant to the U.S. Public Health Service. He is currently a consultant to the Georgia Building Authority where he conducts IAQ investigations and authored the State of Georgia IAQ manual. Since 1980, he has conducted environmental assessments for property owners, developers, mortgage bankers, and insurance companies. In the field of asbestos management and control, he has conducted surveys of over 1500 facilities, including commercial office buildings, schools, hospitals, ships, industrial plants, and government facilities.

During the past 20 years, Mr. Ewing has frequently directed or lectured in training courses sponsored by universities, government agencies, and private interests. Topics have included respiratory protection, asbestos identification, evaluation, management, and control, advanced microscopy, polychlorinated biphenyls (PCBs), heavy metals, air pollution, industrial hygiene, and indoor air quality. He has directed over 50 courses and lectured in over 200 others throughout the continental United States, Alaska, Canada, and Europe.

Mr. Ewing participated in the site assessment of the aircraft carrier *USS Lexington* and development of its environmental management plan prior to its opening as a naval history museum. Much of this work involved PCBs, lead-based paint and asbestos identification and management. Mr. Ewing was responsible for preparing the Safety, Health and Emergency Response Plan (SHERP) and Contractor's Chemical Quality Control Program (CCQCP) for the fire site clean-up at Ft. Huachuca, Arizona. He has also conducted several studies related to flood or fire remediation in commercial and industrial facilities. Since 1988, he has participated in a series of studies designed to evaluate episodic exposures resulting from maintenance and custodial activities in buildings containing asbestos.

Certifications

American Board of Industrial Hygiene (ABIH) Certified Industrial Hygienist, Comprehensive Practice (Certificate No. 2627, Recertified 1990, 1995, 2002)	1983
Indoor Environmental Quality Sub-specialty Exam	1993
Inspector, pursuant to USEPA Asbestos Hazard Emergency Response Act (AHERA) regulations (40 CFR 763, Subpart E, Appendix C), Certificate No. 092, Georgia Institute of Technology; Current Certificate No. 3756-A, The Environmental Institute	1987-Present
Management Planner, pursuant to USEPA AHERA regulations, Certificate No. 083, Georgia Institute of Technology; Current Certificate No. 3756-A, The Environmental Institute	1987-Present
Project Designer, pursuant to USEPA AHERA regulations, Certificate No. 1438, The Environmental Institute; Current Certificate No. 1278-A, The Environmental Institute	1989-Present
Project Supervisor, pursuant to USEPA AHERA regulations, Certificate No. 3400, Georgia Institute of Technology; Current Certificate No. 3891-A, The Environmental Institute	1987-Present
State of Florida, Department of Professional Regulation, Licensed Industrial Hygienist/Asbestos Consultant (No. IA 0000003)	1989-Present

Awards and Honors

Georgia Tech Research Institute Award for Outstanding Performance in Program Development	1983
Commissioned Lieutenant Colonel, Aide de Camp, Governor's Staff by Governor Joe Frank Harris (State of Georgia)	1985
National Asbestos Council, President's Award Recipient	1987
National Asbestos Council, Outstanding Achievement Award	1988
Environmental Information Association, President's Award	1993
Elected Fellow Member Status, American Industrial Hygiene Association	1995
Practices Standards and Guidelines Committee Award, American Industrial Hygiene Association	2005

Memberships

American Industrial Hygiene Association (AIHA)	1978-Present
American Industrial Hygiene Association, Georgia Local Section	1979-Present
American Academy of Industrial Hygiene (AAIH)	1980-Present
American Conference of Governmental Industrial Hygienists(ACGIH)	1992-Present
American Society for Testing and Materials (ASTM)	1992-Present
Environmental Information Association (EIA)	1992-Present
International Society for Indoor Air Quality	1993-Present
National Asbestos Council (NAC)	1982-1992
National Institute for Building Sciences (NIBS)	1988-Present
New York Academy of Sciences (NYAS)	1987-Present

Offices Held

Environmental Information Association Georgia Chapter	
President	1997-1998
American Industrial Hygiene Association	1985-1986
Secretary, Georgia Local Section	
Environmental Information Association	1992-1993
Treasurer	
National Asbestos Council	
Board of Directors	1984-1986, 1988-1991
Secretary	1982-1983
Treasurer	1986-1987

Committees

American Industrial Hygiene Association	
Air Pollution Committee	1983-1984
Asbestos Task Force	1985
Indoor Environmental Quality Committee	1984-1986
Chair	1985-1986
Member/Corresponding member	1992-Present
Chair, Regulatory Affairs Subcommittee	1995-1998
Policy, Standards & Guidelines Committee	1998-2005
Secretary, Vice Chair	2002-2003
Chair, Past Chair	2004-2005
AIHA Journal Peer Reviewer (as requested)	
International Council for Building Research Studies and Documentation	
Task Group for Dissemination of Indoor Air Sciences	1998-Present
National Asbestos Council	
Sampling and Analytical Committee	1984-1986
Professional Registration Committee	1988-1990
Publications Committee	1983-1990
Conference Committee, Chair of Professional Development Courses	1989-1990
San Antonio and Phoenix Conferences	
National Institute for Building Sciences	
Asbestos Task Force	1985-1988
Model Specifications Peer Review Committee (asbestos)	1988-1992, 1994-1996

Lead Based Paint Model O&M Manual Project Reviewer	1994
U.S. Environmental Protection Agency (USEPA)	
Asbestos NESHAP External Advisory Committee	1985-1986
Evaluation of Asbestos Control Technologies (Peer Review)	1985-1987
AHERA Regulatory Negotiation Committee, Invited Technical Advisor	1987
Policy Dialogue on Asbestos in Public and Commercial Buildings, Co-chair of Technical Working Group	1989-1990
Asbestos Strategies Blue Ribbon Committee	2002-2003
Publication Peer Review (USEPA)	
"Measuring Airborne Asbestos Following An Abatement Action" Publication No. EPA 600/4-85-049 (November 1985)	1984-1985
"Guidelines for Conducting the AHERA Clearance Test to Determine Completion of an Asbestos Abatement Project" (1989)	1987-1988
"Guidance for Preventing Asbestos Disease Among Auto Mechanics," Publication No. EPA-560-OPTS-86-002 (June 1986)	1985-1986
"Interim Procedures and Practices for Asbestos Abatement Projects," Publication No. EPA 560/1-85-002 (June 1985)	1984-1985
National Institute for Occupational Safety and Health (NIOSH)	
Publication Peer Review	
"A Guide to Respiratory Protection for the Asbestos Abatement Industry," Publication No. NIOSH/EPA 560-OPTS-86-001 (September 1986)	1985-1986
"An Evaluation of Glove Bag Containment in Asbestos Removal," Publication No. DHHS(NIOSH) 90-119 (October 1990)	1987-1988
Department of the Navy, Naval Facilities Engineering Command	
Publication Peer Review	
"Removal and Disposal of Asbestos Materials," NAVFAC Guide Specification NFGS-02080 (May 1985)	1985
Asbestos Monitor	
Editorial Review Board	1988-1993
City of New York, Department of Environmental Protection (NYC/EPD)	1987-1988
Expert Advisory Board	
American Society for Testing and Materials (ASTM)	
D22 Committee on Sampling and Analysis of Atmospheres	1992-Present
D22.07 Asbestos	1992-Present
E-6 Performance of Buildings	
Subcommittee 23, Lead Hazard Abatement	1994-Present
Health Effects Institute (HEI)	1988-1989
Research Advisory Committee	
Environmental Information Association (EIA)	1992-Present
Editorial Review Board (Peer Reviewer)	1992-1998
Asbestos Committee (Co-Chair)	1998-2000
Building Owners and Managers Association (Asbestos Committee)	1987-1989

US Army Corps of Engineers, Facilities Engineering Support Agency 1984-1985
Publication Peer Review
"Asbestos Management and Control Handbook," TRADOC, Ft. Monroe, VA

Papers and Formal Presentations

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Revised December 1, 2005

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs	CIVIL ACTION NO. 05-40048-FDS
v.	
MARTIN SURFACING, A DIVISION OF SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING; Defendants	

RULE 26 EXPERT REPORT – WILLIAM M. EWING, CIH

At the request of Mr. Mike Hugo and Ian McCallister of Brent Coon & Associates I was asked to review information concerning the resurfacing of the gymnasium in the Field House at Holy Cross to prepare opinions regarding exposures to Coach Dan Allen resulting from this work and related industrial hygiene issues. Industrial hygiene is the field devoted to the identification, evaluation and control of health hazards in the workplace.

I am the Technical Director for Compass Environmental, Inc. located at 1751 McCollum Parkway, Kennesaw, GA 30144-5908. Compass Environmental, Inc. is an industrial hygiene consulting firm that conducts industrial hygiene studies for governmental entities and private companies. Compass also conducts training and research in areas related to industrial hygiene. As Technical Director my responsibilities include preparation of industrial hygiene study designs, conducting field work, preparation of reports and training materials, quality control, and review of other industrial hygienists' work.

My formal education consists of a BS degree in biology from Washington & Lee University (1978) with additional course work in statistics, and technology & science policy at the University of Michigan, Georgia State University, and the Georgia Institute of Technology. I have also completed classes in industrial hygiene, toxicology, respiratory protection, asbestos control, environmental assessments, indoor air quality, and related subjects.

I am certified in the comprehensive practice of industrial hygiene by the American Board of Industrial Hygiene (No. CP 2627). This certification required I complete the core certification examination following at least one year full-time industrial hygiene experience, and the comprehensive practice examination after 5 years of full-time industrial hygiene experience. I passed my core examination in 1980 and my comprehensive practice in 1983. I have maintained my certification since that time and in 2007 my certification was extended until 2012. In 1993 I passed the sub-specialty examination in Indoor Environmental Quality.

I am a member of the American Industrial Hygiene Association (AIHA), the American Conference of Governmental Industrial Hygienists (ACGIH), the National Institute of Building Sciences (NIBS), the American Society for Testing and Materials (ASTM), the International Society of Indoor Air Quality and Climate (ISIAQ), and several other professional or technical organizations. I serve on the AIHA Indoor Environmental Quality Committee and previously was chairman of this committee. I am a member of the AIHA Practices, Standards and Guidelines Committee and served as its chair in 2004. I was recognized as a Fellow Member in 1995 by the AIHA.

I have practiced industrial hygiene for 29 years. Most of my work has focused on the identification, evaluation and control of airborne contaminants. This includes anticipating the release of contaminants during various work activities, determining pathways of exposure, measuring exposures to workers and bystanders, and controlling exposures following the hierarchy of controls concept. As an industrial hygienist I am knowledgeable of general and local exhaust ventilation principles, design and operation. I am familiar with the regulations affecting workers' exposures to chemicals promulgated by the Occupational Safety and Health Administration (OSHA). I am also familiar with recommended practices and guidelines put forth by the National Institute for Occupational Safety and Health (NIOSH), the ACGIH, and other organizations. My CV is attached providing additional information, including a list of my publications. Also attached is a list of my trial and deposition testimony covering the last 5 years. Compass Environmental, Inc. invoices $185 per hour for my time.

To gain an understanding of the facts surrounding the floor resurfacing I was provided the following materials to review.

Affidavit of Paul Crecelius
Affidavit of Paul Bachia
Affidavit of Robert Bradley
Video taken on May 14, 2007 during a visit to the Holy Cross field house
Scott Merrill deposition taken June 14, 2007
Rod Paul deposition taken April 11, 2007
Technician's Manual for the Installation of Versaturf "360" manufactured by Martin Surfacing, Inc.
Technical data, diagrams, and parts lists for Graco, Inc. airless sprayers

Lord Chemical Products, "Troubleshooting & Application Guidelines for Chemglaze Coatings for Synthetic Athletic Floors."
Martin Surfacing, Inc., "Versaturf 360 Monolithic Floor System Specification"
Dan Allen, Personal Medical History (4 pages)
Laura Allen answer to Interrogatory No. 2 (1 page)
Material Safety Data Sheets for Martin Surfacing, Inc. (Bates Nos. HC01532-746)
Additional Material Safety Data Sheets
NOAA Local Climatological Data, Worcester, MA for May and June 2001
Martin Surfacing Pre-Installation Checklist, and other miscellaneous documents with Bates Nos. HCO 1436-1445
Resurfacing Specifications for Urethane Flooring (Bates No. 000179-181)
Martin Surfacing product information for Versaturf 360 (Bates Nos. 000218-220)
Floor (piping) plans (M-1 and M-2) for the Holy Cross field house (2 pages)
Mechanical plans (M-3 and M-4) for the Holy Cross field house (2 pages)
Rule 26 Expert Report of Marcia Ratner, Ph.D. dated June 14, 2007

From my review of these materials it is my understanding that Holy Cross contracted with Martin Surfacing, Inc. (owned by Southwest Recreational Industries, Inc.) to remove the worn infield athletic surface from the field house gymnasium and install a new Versaturf 360 surface. The work apparently occurred over a one to two week period in late May and/or early June 2001. The area to be resurfaced was stated to be 17,000 square feet on the first floor.[1] At any given time there appears to have been no fewer than two, nor more than five contractor employees at the site performing the work. According to Mr. Paul Crecelious, the floor surface was prepared by sanding and then vacuuming to remove loose debris and dust. A primer was then spray applied to the floor surface. After allowing time to dry (probably overnight) the two part polyurethane liquid floor surface material was poured onto the floor and raked out to provide a single seamless membrane when it cured. One or more coatings were then applied to the floor.[2] The final floor, based on the site visit conducted in 2007, was tan in color with white and red lines for the basketball courts. According to Mr. Paul's testimony and Mr. Crecelious' affidavit the workers wore full-face negative pressure air-purifying respirators during the spray operations. To what extent partial or full body protective clothing was worn is unclear. The final steps appear to have been to apply small amounts of primer for the lines and then painting the lines. This final work was done using hand rollers.

The field house was reported originally constructed for the military and physically moved to the Holy Cross campus in the middle of the last century. The total foot print of the building is approximately 25,000 square feet. Most of the first floor is taken up by the gymnasium. A lobby, office area and weight room comprise the remainder of the first level. There are two suites of offices on the second floor comprising about 10,000 square feet. Coach Dan Allen's office was room 214 depicted on drawing M-2. [Note: the rooms have since been renumbered.] One air handling unit was present (and remains) suspended above the gymnasium floor in the northwest corner. This unit is rated at 9705 cubic feet

[1] Deposition of Rod Paul, April 11, 2007, p. 81.
[2] Witness recollections and generic specifications do not agree on how many and exactly which coatings were applied on the Holy Cross job.

per minute (CFM). This is the amount of air it moves to the three office areas it serves on the first and second floors of the field house. The design specifications called for a supply volume to Coach Allen's office of 380 CFM and a return volume of the same amount. The design specifications for the system provided for 2790 CFM to and from the first floor offices. The damper setters per the design would allow for a minimum amount of outside air to be 2275 CFM and a maximum of 9705 CFM. Based on my experience the damper setting was most likely set at 25-50% outside air as an energy conservation measure. The system was designed to be able to both heat or cool the air provided to the office spaces. All return air from all office spaces went to a central mixing box where it was mixed with some outside air, passed through a filter to remove coarse particles, then heated (or cooled), and delivered back to the office spaces through the supply air ducts and diffusers mounted in the ceiling. The air handling unit was apparently operating when the floor resurfacing work occurred. It has not been determined if the system shut down in the evenings.

The open gymnasium area on the first floor relies on natural ventilation. There are approximately 4 or 5 roof-mounted exhaust units that according to Mr. Scott Merrill are equipped with fans. There are three additional exhaust fans in the weight rooms that are designed to pull 11,377 CFM from the gymnasium space into the weight rooms and back into the gymnasium space. It is not clear if any of these exhaust fans were operating during any time the floor was being resurfaced. During the work on the gymnasium floor witnesses reported conflicting accounts on whether exterior (and interior) doors were opened or closed. It appears quite likely that at some times they were opened and at other times closed depending on the work activity, temperature, and need to control the relative humidity during the curing process of the polyurethane. According to various Martin surfacing specifications and the installation manual, the relative humidity should have been maintained below a value of 50 – 68% for a proper cure and prevent a tacky surface. Mr. Paul Crecelious also reported that at some point in the process (after the floor was dry) an industrial exhaust fan was placed in an exterior door to blow the fumes out.

It is not possible to predict with any degree of accuracy the amount of air that moved from the gymnasium to the upper office area where Coach Allen was located based solely on the ventilation design for the building and the conflicting recollections of the witnesses. It is clear that significant concentrations of volatile organic vapors (VOCs) did migrate to Coach Allen's office and other offices on his corridor based on the symptoms experienced by Mr. Allen and his co-workers. The specific symptoms of headache, dizziness, and nausea demonstrate concentrations likely to be well in excess of documented order threshold values reported by the AIHA.[3] Reviewing the Material Safety Data Sheets (MSDS) for the chemicals used during the floor resurfacing, the VOCs would have been in the form of mixtures. This is addressed further below.

[3] American Industrial Hygiene Association (AIHA), *Odor Thresholds for Chemical with Established Occupational Health Standards,* AIHA, Fairfax, VA (1989).

Floor Preparation and Primer

It is not expected the preparation phase of the work that included sanding of the old floor surface would have generated significant VOCs. Some amount of dust would have been generated, however no witnesses indicated that dust was a problem. Once the floor was vacuumed the primer would have been applied. Based on the Martin Surfacing Installation Manual the Martin 2164 Urethane Primer would have been applied undiluted at a rate of 700 square feet per gallon. This material would have been applied with an airless sprayer. According to the MSDS submitted to Holy Cross, the Martin 2164 Urethane Primer contained the following volatile components.[4]

Chemical	Wt. % Less Than	CAS Number
Ethyl benzene	10	100-41-4
Xylene	35	1330-20-7
Methyl Ethyl Ketone (MEK)	45	78-93-3
Toluene	10	108-88-3

Section 9 of the MSDS states the volatile components by weight comprise 89.6% of the primer and section 16 states the volatile organic components comprise 6.45 pounds per gallon. Assuming the workers applied the primer as specified (700 ft^2 per gallon), then 24.3 gallons of primer was used. This would result in the application and subsequent release into the air through evaporation of 24.3 gallons X 6.45 pounds per gallon = 156.7 pounds of volatile components. Using the above percentages, the amount of each volatile component should have been as follows:

Chemical	Lbs.
Ethyl benzene	15.7
Xylene	54.8
Methyl Ethyl Ketone (MEK)	70.5
Toluene	15.7

Polyurethane Floor Membrane

Once this material was allowed to dry (all volatiles organics evaporated) the pouring of the polyurethane floor membrane could occur. According to the materials reviewed, this likely occurred during one day. The polyurethane floor application was performed by metering out the two components of the Versaturf 360 liquid floor surfacing. These two parts are Part A, the resin, and Part B, the hardener. Part A consisted of polyoxy propylene glycol (65%) along with fillers (silica, clays) and iron oxide for color (35%). Part B consisted of a blend of diisocyanates. The machine would pull each part from separate drums and dispense the product into five gallon buckets. The workers would pour the liquid onto the floor and rake it into place forming a seamless floor membrane.

[4] Martin Surfacing, Inc., Material Safety Data Sheet for 2164 Urethane Primer, 2/20/94, Bates Nos. HC01592-96. Note page 1 of the MSDS is missing, constituents derived from section 15 on page 6.

These materials are designed to react to form the urethane polymer comprising the floor as it cures. The components of these chemicals are not very volatile. Apparently the workers performing this work did not wear respiratory protection. Considering the low Threshold Limit Value (TLV) for the diisocyanates this was probably not prudent, however, it is unlikely there was any significant concentration in areas outside the gymnasium proper. Furthermore, the concentration of diisocyanates in the gymnasium was likely quite low as well.

Primer for Urethane Coating

Once the urethane membrane had set (but not completely cured) the primer could be applied prior to the top coat. The material called for in the installation manual, and matching the MSDS submitted to Holy Cross was the Martin A.P. Concentrate. This material was mixed at a rate of 1 part A.P. Concentrate to 4 parts solvent. The solvent, referred to as Martin Blend, consisted of a 50/50 mix of xylene and cellosolve acetate (also known as 2-ethoxyethyl acetate). According to the installation manual the application rate for this primer is 400-800 ft^2 per gallon. Accordingly it would have required 21-43 gallons of the mixed primer to cover the 17,000 ft^2. This corresponds to 4-9 batches of five gallons each. Based on the constituents listed, considered volatile, listed below are the range of quantities of VOCs that would have been emitted during this phase of the floor resurfacing work.[5] The weight percent reported in the MSDS was used with the weight of VOCs per gallon reported in section 16 of the MSDS of 3.82 lbs/gal to complete the following table.

Chemical	Min. (gal.)	Max(gal.)	Lbs. (Min.-Max)
Xylenes (in solvent & concentrate)	8.8	19.8	33.6 – 75.6
Cellosolve acetate	8.0	18.0	30.6 – 68.8
Toluene	0.8	1.8	3.1 – 6.9
Ethyl benzene	0.16	0.36	0.6 – 1.4
Methyl isobutyl ketone (MIBK)	0.16	0.36	0.6 – 1.4
1-methoxy-2-propyl acetate	0.12	0.27	0.5 – 1.0

Apparently during the spray application of this primer the floor surfacing workers wore full-face negative pressure air-purifying respirators equipped with organic vapor cartridges.[6]

Urethane Coating

After allowing the primer to dry, a urethane coating was applied over the new floor. Based on the final floor color (tan) and the submittal to Holy Cross, the coating was likely Martin Surfacing, Inc. S2951 Tan Flat urethane coating. The application rate was

[5] Note: Calculation is based on the percentages reported in the MSDS for A.P. Concentrate. Toluene-2,4-diisocyanate (TDI) present in the concentrate at 1% was not included as it would not be considered volatile to the extent that it might present a significant exposure to persons outside the gymnasium.
[6] Rod Paul deposition of April 11, 2007, p. 26.

likely 125 ft^2 per gallon.[7] For the 17,000 ft^2 floor surface this would have required 136 gallons of tan urethane coating. The percent volatile (by weight) for this compound is stated as 63.3% and the percent volatile by volume as 72.8%.[8] Based on the constituents listed in the MSDS it appears these are reversed and the actual percent volatile by weight is 72.8%. Based on the application rate the quantity of VOCs released during this process should be as follows. The weight of VOCs in the table below is based on the MSDS VOC concentration of 5.43 lbs/gal reported in the MSDS using the 136 gallons applied using the calculation 139 lbs. X 5.43 lbs/gal X weight percent of each component.

Chemical	Gal.	Lbs.	CAS Number
Ethyl benzene	6.8	36.9	100-41-4
Methyl isobutyl ketone	13.6	73.8	108-10-1
1-Methoxy-2-propyl acetate	34.0	184.5	108-65-6
Toluene	13.6	73.8	108-88-3
Xylene	27.2	147.6	1330-20-7
Dipropyleneglycol methyletheracetate	5.4	29.5	88917-22-0

In the above list I did not include the titanium dioxide (opacity filler) or the unspecified coloring agent as these would not be volatile. I also did not include the two isocyanates or the catalyst assuming they would have reacted completely in the mixture. Again, the floor coating workers would have wore the full-face negative pressure air-purifying respirators during the application of the urethane coating with the airless sprayer. This process should have occurred during a single shift and likely allowed to dry overnight.

Game Line Application

The last step in the floor surfacing would have been to measure and tape the game lines. Once the tape was down, a game line paint primer (Martin Surfacing, Inc. Primer 2169) would have been applied with a roller.[9] Once the primer dried (at least 4 hours, or more likely overnight) the game lines were painted using a roller. The white lines were probably painted using Martin Surfacing, Inc. S2107 White Coating.[10] The red lines were likely either Martin Surfacing, Inc. Aviation Red/Flat or Track Brick/Red Flat coating.[11] While each of these primers and paints contain VOCs the actual amount of coverage in square feet would have been small, with relatively small releases of VOCs.

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[7] Martin Surfacing Installation Manual at page 33 describes mixing and spraying the urethane coatings. This manual allows for three different procedures. The procedures all would result in similar releases of the same VOCs during application, although the 25 gallon batch process would result in some additional forms of VOCs from the solvent used.

[8] Martin Surfacing, Inc., Material Safety Data Sheet, S2951 Tan Flat, Bates Nos. HC01619-24.

[9] Martin Surfacing, Inc. Installation Manual, p. 36.

[10] Martin Surfacing, Inc., Material Safety Data Sheet, S2107 White Coating, Bates No. HC01713-19.

[11] Martin Surfacing, Inc. Material Safety Data Sheets (3) at Bates Nos. HC01669-92.

Other Solvents

I also recognize that additional quantities of solvents were used by Martin Surfacing, Inc. employees to clean and flush the application equipment. Which solvents were used, in what quantities, and what was done with the solvent waste has not yet been determined.

Based on this understanding of the activities that occurred during the floor resurfacing in the field house there was likely three separate days when major releases of VOCs occurred. These were the two primer applications and the urethane coating application. There were at least three pathways of exposure to the upper offices where the symptoms were expressed by Coach Allen and his co-workers. One pathway was via the first floor offices that would return air to the air handler mixing box and redistribute that air to the three office areas. The second would be through leakage into the return air duct and points upstream of the air handling unit fan located in the gymnasium proper. The third pathway would be through simple migration from space-to-space.

The symptoms of headaches, dizziness and nausea are classic for overexposure to xylenes, toluene, methyl ethyl ketone, ethyl benzene, and methyl isobutyl ketone. The amounts released into the air of the building were not trace amounts, but hundreds of gallons representing hundreds of pounds of these compounds. Likewise, the symptoms associated with excessive exposure to acetates, such as the cellosolve acetate, according to the OSHA data sheet for this compound include headaches, dizziness, and nausea.[12] It is likely the reported symptoms were from exposures to the combination of VOCs in about the same ratios as used during the floor installation.

Ambient Climatological Data

During the preparation of this report I reviewed the climatological data for May and June 2001. Summarized below are the findings for temperature and percent relative humidity during the last ten day of May and the first ten days of June.

Ambient Temperature and Relative Humidity for Worcester, MA during May 22 – June 10, 2001[13]

Date	Temperature (F)			Average Wet Bulb (F)	Relative Humidity (%)	Comments
	High (F)	Low (F)	Average (F)			
5/22	52	48	50	50	100	Rain, Heavy Fog, Mist
5/23	57	47	52	46	65	Rain, Heavy Fog, Haze
5/24	62	47	55	46	50	Rain, Mist, Haze
5/25	64	46	55	49	67	Rain
5/26	68	48	58	53	72	Rain, Mist

[12] Occupational Safety and Health Administration (OSHA), Data Sheet for 2-Butoxyethyl acetate (available at www.osha.gov).
[13] National Oceanographic & Atmospheric Administration (NOAA) National Climatic Data Center, Worcester Regional Airport Station.

5/27	58	54	56	N.D.	N.D.	Rain, Heavy Fog, Mist
5/28	69	51	60	N.D.	N.D.	Rain, Mist
5/29	67	49	58	53	72	Rain
5/30	57	42	50	44	64	Rain
5/31	61	39	50	44	64	
6/1	69	43	56	48	58	
6/2	65	51	58	N.D.	N.D.	Rain, Heavy Fog, Mist, Haze
6/3	64	51	58	N.D.	N.D.	Rain, Heavy Fog, Mist, Haze
6/4	64	50	57	53	77	
6/5	69	50	60	55	72	
6/6	71	54	63	55	61	
6/7	74	53	64	46	22	
6/8	76	56	66	54	46	
6/9	76	59	68	55	43	
6/10	79	58	69	57	48	

N.D. = No data

Good industrial hygiene practices call for the identification, evaluation and control of health hazards in the workplace. The application of polyurethane floor surfaces provides numerous opportunities for workers' exposure to various organic compounds (specific ones described above) and to the diisocyanates. Martin Surfacing, Inc. was required under the OSHA regulations to conduct air sampling during this project, unless they had accumulated a large quantity of data from many other substantially similar projects. The purpose for this sampling is to determine if the personal protective equipment (e.g., respirators) provided to workers is providing adequate protection. It is odd that the MSDS for these products state that if you spill the product, a self-contained breathing apparatus (SCBA) should be used for clean-up. However, here the workers were intentionally spraying the products (hundreds of gallons) onto the floor while wearing only full-face negative pressure air-purifying respirators. At the time, SCBA was rated with a protection factor of 10,000 and the full-face air-purifying respirator was rated at 50. This means the SCBA should reduce the exposure by a factor of 10,000 while the other by a factor of 50, if properly fit-tested and used by properly trained workers.

When conducting sampling the results are generally compared against the OSHA permissible exposure limits (PELs), the ACGIH Threshold Limit Values (TLV), or other guidelines. It should be noted that when there are exposures to multiple exposures to different chemicals that have effects on the same target organs or systems the industrial hygienist considers the exposure to the entire mixture. This is explained by the ACGIH as follows:

When two or more hazardous substances have a similar effect on the same target organ or system, their combined effect, rather than that of either individually, should be given primary consideration. In the absence of information to the contrary, different substances should be considered as additive where the health effect and target organ or system is the same. That is, if the sum of

$$C_1/T_1 + C_2/T_2 + \ldots C_n/T_n$$

exceeds unity (one), the threshold limit of the mixture should be considered as being exceeded (where C_1 indicates the observed atmospheric concentration and T_1 is the corresponding threshold limit.)[14]

Another reason for conducting air sampling is to determine what exposures may result to bystanders by the floor surfacing work. In a multiemployer worksite, such as the field house when the floor was being resurfaced, the responsibility for worker health and safety is different than when only one employer is present at a worksite. An employer that creates a hazard by their activities has responsibility for their own employees as well as others that might be affected by the hazard. Employers also carry responsibility for the health and safety of their own employees. Lastly, the workers themselves are responsible to use the protective equipment they have been provided (and trained to use), and follow the work practices they have been trained to use.

I have requested any air sampling data that might have been collected during the floor resurfacing project at the field house in 2001. I have also requested any air sampling data from other jobs that Martin Surfacing, Inc. performed while installing polyurethane floor surfacing. I understand none were taken at the Holy Cross field house project.[15] I have not seen any from any other Martin Surfacing, Inc. projects and do not know if any exist. Without air sampling data it is difficult for an employer to evaluate the extent of the hazard posed to workers and how to control those hazards.

To control a hazard industrial hygienists rely upon a concept know as the hierarchy of controls. The first choice is to eliminate the hazard through substitution. This could include the elimination of a hazardous material, or selection of a less hazardous substance, if feasible. For example, Martin Surfacing, Inc. MSDS sheets for some of their paints used on athletic surfaces contained high concentrations of lead. They should not have still been using lead and lead chromate paints. Martin Surfacing, Inc. should have investigated using substitute solvents and a substitute for the isocyanates. I do not know whether they did this at some point or not.

If a hazard cannot be eliminated through substitution, every effort should be made to engineer out the hazard. The use of engineering controls greatly reduces the chance of human error. Segregation of the work, enclosures, and local exhaust ventilation are typical examples.

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[14] ACGIH, *2006 TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices,* ACGIH, Cincinnati, OH (2006), p. 85

[15] Note: I understand some air sampling was conducted approximately 15 months later in the field house. It is unlikely these results, should they become available, will be helpful in retrospectively establishing exposures from May — June 2001.

Work practices designed to reduce exposures should always be used where feasible. For example, a paint roller can be used to apply the primer instead of an airless sprayer. Administrative controls can also be used. For example, the work resulting in possible exposures to bystanders can be done when those persons are not present (after hours).

The last choice in the hierarchy of controls is to put workers in respirators. The respirator becomes the last line of defense for an inhalation hazard. For a tight-fitting full-face air-purifying respirator, such as that worn by some workers at the field house project, to be effective, it must be properly fitted and the workers enrolled in a respiratory protection program. The workers must be trained and understand that facial hair, or even a couple of days without shaving, can compromise the seal between the mask and the face greatly reducing the effectiveness of the device.

One of the most important elements of an effective industrial hygiene program is education of the worker. The workers need to know the extent of hazards associated with their work and how to protect themselves. This is usually done through an effective hazard communication program as described in the OSHA standard at 29 CFR 1910.1200. If workers need to wear respirators, they also need training in respiratory protection as described at 29 CFR 1910.134. Workers wearing a respirator must first have a medical determination to be certain they are capable of wearing a negative pressure device without impairing their health.

According to Mr. Rod Paul, Martin Surfacing, Inc. never did worker training.[16] The standard practice appears to have been to have two Martin Surfacing, Inc. employees go to a job site and hire local laborers on a temporary basis to perform much of the work.

As part of my review I searched the on-line OSHA site inspection database for previous OSHA inspection results at Martin Surfacing (or Southwest Recreational Industries) projects. In 1992, Martin Surfacing, Inc. was cited for violations to the OSHA standards regarding personal protective equipment, particularly eye and face protection. In a separate inspection at the same job location they were cited for violating the hazard communication standard. At another project they received three serious citations for violating the hazard communication standard, material safety data sheets, and respiratory protection. In another project in Alexandria, VA they were cited for failure to perform chemical monitoring. These all occurred prior to the Holy Cross project. In August 2002 Southwest Recreational Industries, Inc. was issued nine citations including violations of the hazard communication standard, material safety data sheet violations, personal protective equipment violation, respiratory protection standard violations, medical records access violation, and the failure to provide employee information and training, among others.

In summary, it is my opinion to a reasonable degree of scientific certainty that Coach Dan Allen and some of his co-workers present in the field house during the gymnasium floor resurfacing were exposed to significant concentrations of solvent vapors during at least three days of the work. Based on the information reviewed to date, it is not possible for

[16] Rod Paul deposition of April 11, 2007, p.10.

me to conclude whether Mr. Allen's exposure to any particular chemical was in excess of the PEL or TLV. However, it is likely that Mr. Allen's exposure to this mixture of solvents known to act on the central nervous system approached or exceeded the PEL and TLV for the mixture.

William M. Ewing

William M. Ewing, CIH

June 21, 2007

Date

RICHARD W. CLAPP, D.Sc., MPH
Email: rclapp@bu.edu

EDUCATION

D.Sc.	Boston University School of Public Health, Epidemiology, 1989.
M.P.H.	Harvard School of Public Health, Health Services, 1974.
B.A.	Dartmouth College, Biology, 1967.

EXPERIENCE

2004-present **Senior Environmental Health Scientist, Environmental Health Initiative, Lowell Center for Sustainable Production, School of Health and Environment, University of Massachusetts, Lowell.**
Conducts and supervises epidemiologic data analyses, literature reviews and technical assistance in community-based environmental health studies. Works on other environmental health projects and training activities as required.

2002-2004 **Senior Environmental Health Scientist, Sustainable Communities Group, Tellus Institute.**
Responsible for the development and conduct of studies concerning the health effects of environmental toxic exposures in communities. Provided expert advice and training programs for citizens groups and interested professionals. Assisted in the strategic planning and development of the Environmental Health Program in the Sustainable Communities Group at Tellus.

2002-present **Professor, Boston University School of Public Health, Boston, MA**
1995-2002 **Associate Professor, Boston University School of Public Health, Boston, MA.**
1992-1995 **Assistant Professor, Boston University School of Public Health, Boston, MA.**
Teaches courses in environmental health and environmental epidemiology to masters and doctoral level graduate students. Advises doctoral students on dissertations in environmental health and epidemiology. Participates in departmental committees and research activities, including assessment of health effects of nuclear weapons production, environmental and occupational toxic exposures.

1989-1994 **Director, Center for Environmental Health Studies, JSI Research & Training Institute, Boston, MA.**
1995-2002 **Consultant - JSI Research & Training Institute, Boston, MA**
Responsible for development and conduct of studies of health effects of environmental toxic exposures in communities. Coordinated consultants from Boston University School of Public Health Environmental Health Department providing expert advice and training programs for citizens groups and interested professionals. Managed personnel and budget for variety of projects.

1980-1989 **Director, Massachusetts Cancer Registry, Massachusetts Department of Public Health, Boston, MA.**
Responsible for establishing statewide cancer incidence reporting system, coordinating reports from over one hundred fifteen hospitals and licensed clinics, and centralizing information in computerized database. Supervised staff and consultants involved in data

editing, quality assurance and data reporting activities. Worked with broad-based advisory committees, citizens groups, and epidemiologic researchers conducting studies of cancer incidence in Massachusetts. Involved in numerous Department of Public Health committees and research projects, including leukemia in Woburn, and other cities and towns. Participated in regional and national organizations of cancer registry directors.

1979-1980 **Acting Director of Occupational and Environmental Health Studies, Equifax Health Systems Division, Reading, MA.**
Participated in epidemiologic feasibility study of health effects of low-level ionizing radiation, review of OSHA health standards for lead, cotton dust, and asbestos, review of comments on Federal inter-agency carcinogens policy. Supervised staff involved in evaluating union-based occupational health education grant and surveying U.S. population-based cancer registries.

1977-1978 **Director, Childhood Lead Poisoning Prevention, Massachusetts Department of Public Health, Boston, MA.**
Supervised laboratory, office, field inspector and legal staff of statewide program involved in screening for lead poisoning and investigating possible environmental sources of lead. Coordinated development of job training programs for unemployed persons in the areas of lead paint inspections and lead hazard abatement in dwellings. Reported to Governor's Committee on Childhood Lead Poisoning and managed diverse personnel and budgets. Presented educational programs and videotaped training sessions on childhood lead poisoning.

1975-1976 **Executive Director, Lynn Community Health and Counseling Center, Lynn, MA.**
Responsible for overall management of multi-service center offering comprehensive pediatric and adolescent health services, family planning services, childhood lead poisoning prevention services, individual and family counseling, social service advocacy and a day activity program for mentally retarded adults. Worked with other human services agencies in developing a WIC program, and participated in regional and state-level health planning activities. Reported to community board and managed diverse personnel and budgets.

1974-1975 **Manager, Pediatric and Psychiatric Group Practices, Massachusetts General Hospital, Boston, MA**
Managed conversion of out-patient clinics to hospital-based group practices with salaried staff as part of developing Ambulatory Care Center. Implemented cost centers and program planning and budgeting system and reported to Medical Directors of two specialty groups.

1972-1974 **Deputy Director, Prison Health Project, Massachusetts Department of Public Health, Boston, MA.**
Hired medical and ancillary health staff for five state prisons, supervised survey of prison health conditions in county and municipal correctional facilities, and coordinated establishment of two community-based alternative programs for inmates convicted of drug-related crimes. Established twenty-four hour emergency coverage for maximum security prison, and worked with inmate medical advisory committees at several facilities.

1970-1972 **Program Research Analyst, New York City Health Services Administration, New York, NY**

Analyzed public health programs in City Hospitals, the prison hospital and Houses of Correction. Made recommendations regarding improved operations and staffing levels. Drafted guidelines for affiliation agreement for teaching hospital administration of Riker's Island prison medical services.

TEACHING APPOINTMENTS

2004-Present	Adjunct Professor, University of Massachusetts –Lowell.
2002-Present	Professor, Boston University School of Public Health.
1995-2002	Associate Professor, Boston University School of Public Health.
1993-1995	Assistant Professor, Boston University School of Public Health.
1990-1993	Adjunct Assistant Professor, Boston University School of Public Health.
1989-1995	Assistant Clinical Professor, Tufts University School of Medicine

PUBLICATIONS

Clapp R. Polychlorinated biphenyls. In: Last's Public Health and Preventive Medicine, 15th ed. (in press)

Clapp RW, Howe G, Jacobs M. Occupational and Environmental Causes of Cancer. Encyclopedia of Public Health (submitted).

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PRESENTATIONS

"Mortality in a large computer manufacturing company, 1969-2001." American Public Health Association Annual Meeting, Boston, 2006.

"Recent Epidemiologic Evidence of the Carcinogenicity of Dioxin." American Public Health Association Annual Meeting, Philadelphia, PA, 2005.

"Pesticides and Child Development in Rural KwaZulu-Natal. International Society for Environmental Epidemiology, Johannesburg, SA, 2005.

"Uses and Mis-uses of Epidemiology in Torts." International Society for Environmental Epidemiology Annual Meeting, NY, NY, 2004.

"PCBs, Dioxins and Cancer – an Update." Cancer Prevention Rounds. Boston University School of Medicine, Boston, MA, 2003

"Cancer Incidence in Massachusetts Persian Gulf War Veterans." International Society for Environmental Epidemiology Annual Meeting, Vancouver, British Columbia, 2002.

"Health Impacts of the Nuclear Fuel Cycle." Epidemiological Society of Southern Africa Annual Meeting, East London, South Africa, 2000.

"Childhood Leukemia in Woburn, MA: Science, Politics and Policy." International Society for Environmental Epidemiology Annual Meeting, Athens, Greece, 1999.

"Incidence of Malignancy in Populations Adjacent to the Pilgrim Nuclear Reactor." Symposium on Recent Studies of Low-Level Radiation and Implications for Medicine and the Nuclear Industry, New York City, 1998.

"Cancer Surveillance of Massachusetts Veterans, 1988-1993". North American Association of Central Cancer Registries Annual Conference, Boston, MA, 1997.

"Update of Cancer Incidence in Massachusetts Veterans, 1988-1993." International Society of Epidemiology in Occupational Health Annual Meeting, Harare, Zimbabwe, 1997.

"The Upper Cape Cancer Incidence Study". Sixth Annual Symposium on Environmental and Occupational Health during Societal Transition in Central and Eastern Europe, Eforie Nord, Romania, June, 1995.

"Popular Epidemiology." Loka Institute Conference on Dissenting Ways of Knowing, University of Massachusetts, Amherst, MA, 1994.

"Agency Responses to the Woburn Leukemia Cluster". Fifth Annual Symposium on Environmental and Occupational Health during Societal Transition in Central and Eastern Europe, Nitra, Slovak Republic, 1994.

"New Carcinogen Threshold Theories: Implications for Prevention," University of Connecticut conference on Incorporating Molecular Mechanisms into Estimates of Cancer Risk, 1992.

"Angiosarcoma, porphyria cutanea tarda and probable chloracne in a worker exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin-contaminated waste oil," Twelfth International Symposium on Dioxins and Related Compounds, Tampere, Finland, 1992.

"Occupation and Race Data in Central Cancer Registries," American Public Health Association Annual Meeting, Atlanta, 1991.

"Respiratory Cancer by Race and Gender: Selected Occupational Associations in Massachusetts, 1982-85," National Minority Health Conference, Atlanta, 1990.

"Statistical Methods for Analyzing Cancer Clusters." National Conference on Clustering of Health Events, Atlanta, GA, 1989.

"Cancer Statistics and the Right to Know". American Public Health Association Annual Meeting, Boston, 1988.

"Respiratory Disease Mortality and Morbidity, Respiratory Cancer and Mesothelioma Incidence: Occupational Associations in Massachusetts, 1982-1985." American Public Health Association Annual Meeting, Boston, 1988.

"Soft Tissue Sarcoma Incidence in Massachusetts Vietnam Veterans, 1982-1986." American Public Health Association Annual Meeting, Boston, 1988.

"Dealing with Cancer Clusters." American Association of Central Cancer Registries founding meeting, Chicago, IL, 1988.

"Cancer Surveillance in Massachusetts, 1982-1983." International Association of Cancer Registries Meeting, Hartford, CT, 1985.

OTHER INVITED PAPERS

"Occupational and Environmental Causes of Cancer." Second International Congress of the Paris Appeal, Paris, France, 2006.

"Occupational and Environmental Causes of Cancer." Collaborative on Health and Environment Annual Meeting, San Francisco, CA, 2006.

"Industry Influence in the EPA Dioxin Reassessment." Center for Science in the Public Interest, Washington, DC, 2004.

"The U.S. War on Cancer." Cancer, Environment and Society conference, ARTAC/UNESCO, Paris, France, 2004.

"Epidemiology in Toxic Torts." Environmental and Occupational Health Sciences Institute, Robert Wood Johnson Medical School, Piscataway, NJ, October, 2000.

"Global Climate Change and Health." Grand Rounds, Dartmouth Medical School, Lebanon, NH, December, 1999.

"PCBs in Massachusetts: Is There a Cancer Risk?" Cancer Prevention Rounds, Boston University School of Public Health, January, 1998.

"Epidemiologic Studies of the Woburn Childhood Leukemia Cluster." American College of Occupational and Environmental Medicine Annual Meeting, April, 1998.

"Agent Orange and Veterans Health - 1996 Update." Occupational Health Program, Harvard School of Public Health, Boston, March, 1997.

"Surveillance of Cancer in Massachusetts Veterans, 1988-1993." Tumor Registrars Association of New England, St. Elizabeth's Hospital, May, 1997.

"Health Effects of U.S. Nuclear Weapons Production". Slone Epidemiology Unit, Brookline, MA, June, 1997.

"Agent Orange and Veterans Health - 1996 Update." Public Health Forum, Boston University School of Public Health, Boston, November, 1996.

"Agent Orange and Cancer". Cancer Prevention Rounds. Boston University Medical Center, Boston, MA, 1994.

"Patterns of Cancer in Vietnam Veterans". Hematology/Oncology Rounds. Massachusetts General Hospital, Boston, MA, 1991.

"Agent Orange, Health Effects and Government Policy". Health and the Environment Lectureship. Brown University, Providence, RI, 1991.

"Cancer Surveillance of Vietnam Veterans in Massachusetts". Distinguished Lecture Series in Occupational Medicine. Robert Wood Johnson Medical School, Piscataway, NJ, 1989.

HONORS AND AWARDS

Science for the Benefit of Environmental Health. B.U. Superfund Basic Research Program, 2006
Member, Harvard School of Public Health Occupational Health Program Advisory Committee, 2000-Present
Vice-Chair, Greater Boston Physicians for Social Responsibility Steering Committee, 1999-Present
Chair, Massachusetts Toxics Use Reduction Institute Science Advisory Board, 1994-1996; Member, 1994-2003
Marla Frazin Award, Massachusetts Breast Cancer Coalition, 2002
Public Scientist of the Year Award, Association for Science in the Public Interest, 2001
Member, International Society for Environmental Epidemiology Governing Council, 2001
Member, Harvard School of Public Health Alumni Council, 1997-1999
Award for Public Health in the Work Environment, University of Massachusetts Lowell, 1997
Member of Massachusetts Advisory Board on Toxics Use Reduction, 1990-1994
Lemuel Shattuck Award, Massachusetts Public Health Association, 1990
Environmental Health Network 1990 National Award

PROFESSIONAL MEMBERSHIPS

- American Public Health Association
- Massachusetts Public Health Association
- MassCOSH
- American College of Epidemiology.
- Society for Epidemiologic Research
- Harriet Hardy Institute
- International Society for Environmental Epidemiology

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION NO. 05-40048-FDS

RULE 26 EXPERT REPORT - DR. RICHARD W. CLAPP, D.Sc., MPH

1. My name is Richard Clapp and I have been asked to provide a rebuttal report in this matter by the law firm of Kreindler & Kreindler, LLP.

2. I am a Professor at the Boston University School of Public Health, at 715 Albany Street, Boston, MA where I am employed as Professor in the Department of Environmental Health.

3. I have received academic training as a public health professional and epidemiologist. I received a Master of Public Health degree from the Harvard School of Public Health in 1974 and a doctoral degree in Epidemiology from the Boston University School of Public Health in 1989. My area of specialization in my doctoral program was cancer epidemiology. A current copy of my curriculum vitae is attached to this affidavit.

4. I have reviewed the reports in this matter by Dr. Dean Hashimoto dated May 24, 2007 and Dr. Marcia Ratner, dated June 14, 2007. I have paid particular attention to the methods they used to reach their conclusions and compared their method to standard approaches used by epidemiologists to assess causal associations.

5. The guidelines, perspectives and tools for epidemiologists to come to a general assessment of whether or not there exists a causal connection between workplace or environmental exposures, and latent disease have been developed over the past forty

years. The widely recognized and useful "Hill guidelines," which Professor Austin Bradford Hill offered in 1965, are set forth and explained below.

6. Epidemiologists concerned with the causes that contribute to human disease risk routinely use the Hill guidelines or "viewpoints" as a set of useful tools for drawing scientific inferences and deductions about causation from all the available relevant principles, data, information, and observations. 1 I present here a discussion of how epidemiologists inquire into the contributions of the environment, including the workplace environment, to causing disease.

7. Scientific practice is taken up with more than exploring questions of causation, but this is a central question in many tort cases. What does "A causes B" mean to a scientist? Apart from philosophical aspects of scientific causality, most scientists have adopted a pragmatic approach whose formal articulation goes back at least to John Stuart Mill's famous "Method of Difference."2 Briefly, Mill's Method holds that A causes B if, all else being held constant, a change in A is accompanied by a subsequent change in B. The formal method to detect such an occurrence is the Experiment, whereby:

- all things are held constant except A and B,
- A is varied, and
- B observed.

8. Not all sciences can utilize a strictly experimental method, however. Some scientists must be content to make observations of the real world and deduce scientific fact by applying reasoning and principles from experimental sciences or logic and mathematics. Astronomy, geology, and epidemiology are such sciences but the first two generally reach conclusions by deducing from observations rather than conducting controlled experiments. The inability of geology or astronomy to conduct full-scale experiments does not connote an inability to do good science, or that the science involved is inherently more "error prone" or less reliable than a branch of science that can conduct full-scale experiments.

9. Scientists may, however, extrapolate from laboratory scale experiments to make scientifically defensible statements about the origins of a "black hole" in space or the causes of earthquakes on our planet. There may be disagreement among experts as to the aptness of a particular extrapolation or inference, but generally there is no disagreement that the process of applying events or principles observed on the scale of the laboratory bench to events occurring on the scale of a geographic region is scientifically defensible, and indeed something similar is the norm in virtually all observational sciences.

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1 The historical context of these guidelines is of interest: Sir Bradford Hill proposed his viewpoints in 1965, well before the International Agency for Research on Cancer (IARC) or U.S. agencies such as the EPA or OSHA had begun promulgating lists and categories or carcinogens. Further, Dr. Bradford Hill's own commentary on the use of his guidelines was most instructive: they are not meant to replace common sense and judgment but to aid them.

10. In the biological sciences, in general, and in the public health field, in particular, inferences for one group of humans are regularly drawn from epidemiological studies from another group of humans. Significantly, inferences about humans are also made on the basis of observations of, or test-tube experimentation, on animals. Indeed, the scientific reasonableness of drawing inferences from animals to humans provides the principal justification for the decision of National Institutes of Health to devote hundreds of millions of dollars funds to animal research. Any particular inference may be arguable, and certainly may be the basis of a dispute between the parties in a lawsuit, but the method and reasoning are not subject to debate.

11. In general there are three sources of information on the effects of toxic exposures in human beings: (a) case reports, (b) toxicological research (including both animal studies and chemical/structural research), and (c) epidemiological studies.

(a) The use of case reports regarding the effects of toxic exposures in human beings – A case report, i.e.,, a report in the medical or scientific literature of a single case or series of cases, are one of the most important sources of information scientists have on effects of toxic substances, and often the only source of information. Detailed reports of cases of accidental poisonings or suicides provide information, such as autopsy data, biopsies and detailed clinical data, not obtainable by any other route. Moreover they constitute important and obvious "natural experiments," experiments where the relationship between the exposure and effect is usually clear. The use of case reports in medicine is longstanding and important, as evidenced by the continued appearance of such reports in the literature3. Indeed the logic of a case report is similar to that of a more formal case-control or cross-sectional study.

(b) The use of toxicological research reports to understand the effects of toxic exposures in human beings – Toxicological research (including both animal studies and chemical/structural correlations), along with epidemiology, is one of the two other sources of information provides much of the basis for scientific judgments relating toxic exposures to health effects.

(c) Epidemiological studies are observations of "natural experiments" that are occurring in the real world. The idea is to find situations which are almost like laboratory experiments, observe them, obtain as much information as possible from them, and then interpret the results. The essence of the natural experiment in epidemiology is almost always a comparison

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3 The Lancet, for example, one of the world's leading medical journals, contains a Case Report every week.

> between groups, for example, a group exposed to a chemical and one not exposed. The ideal situation would be to have the groups in the real world the same in all relevant respects (i.e., comparable) except for the variable under study. Unfortunately such natural groupings are rarely comparable, and techniques must be used to account for known differences.

12. Toxicology is an experimental science, while epidemiology is an observational science. The advantages of being able to conduct an experiment are obvious. Because John Stuart Mill's famous Method of Difference depends upon observing the result on B of a change in A, other factors must be held constant. The essence of an Experiment is the control of all factors, except for A and B. This kind of control allows the scientist to ask quite precise questions about explicitly defined A's and B's, and get relatively unambiguous answers. 4

13. However, not all sources of non-comparability are known. If not a necessary accompaniment of the variable being investigated, these residual factors fall by chance in the two groups being compared. The result is that there are usually differences solely attributable to the random way these factors are distributed between groups in the particular study. The "chance" fluctuations in apparently otherwise similar populations require an epidemiologist to use statistical tools to evaluate the role of "noise" that might be obscuring an underlying "signal."

14. Observing some unintended or "natural" experiment in the real world, which is the essence of observational sciences like epidemiology, has the enormous advantage that it involves human beings living under conditions similar to ones found by plaintiffs in a personal injury suit. Nonetheless, questions inevitably arise about the biological/scientific comparability (and thus the legal relevance or "fit") of the people and exposures and diseases studied in one place and time and other people at other places and times. For example, questions such as whether the comparison of the cases and controls was truly comparing "like with like," which is precisely the kind of problem that can be and generally is avoided in a tightly controlled experimental study.

15. Thus, as my colleague Dr. David Ozonoff explained in detail in a 1994 peer reviewed article, toxicological experiments and epidemiological studies each have characteristic strengths and weaknesses. 5

16. In view of the fact that different scientific disciplines have disparate strengths and weaknesses, and the propensity of scientists to disagree, the key question for scientists – and courts – becomes determining how scientists decide which studies and data and experiments and articles to use and rely and for what purposes, i.e., how do they interpret and apply the results of scientific studies?

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4 Whether complete control is practically possible varies, of course, but the principle should be clear.

5 Ozonoff, D "Conceptions and Misconceptions about human Health Impact Analysis" Environment Impact Assessment Review, 14, 499-516, 1994.

17. It is well known that when different scientists interpret the same studies they do not always reach the same conclusion. How and why do scientists interpret the "same" basic facts, the same set of numbers, the same research report, in different ways? Two aspects and tools of scientific interpretation are relevant to this discussion. In the literature of scientific methodologies they are commonly (but not invariably) referred to as internal and external validity.

18. Internal validity refers to a judgment about the extent to which the experiment or study produces valid information on its own terms, i.e., the extent to which it is internally valid. Thus, for internal validity the crucial question to be answered is not, "If toluene causes damage to the brains of rats, does it also do so in mice or humans?" but rather "Did the experiment validly show that toluene caused brain damage in rats?"

19. External validity, on the other hand, refers to a judgment about the extent to which the internally valid results of an experiment or study can be generalized to other situations, and to which ones. Thus, for external validity the crucial question to be answered is not "did the experimental evidence adequately demonstrate that damage brain cells in rats?" but rather "If toluene causes brain damage in rats, does it also do so in humans?"

20. Once an unusual event is observed or an unexpected experimental result is obtained it remains to explain or interpret the observation or result, whether the result is a difference or a lack of a difference in the expected or compared entities.

21. Take as an example a study comparing the health outcome of two distinct groups of human beings, one group comprised of those workers in a factory who were exposed to a chemical used in the production process, and the other group consisting of all members of the general population, most (but perhaps not all) of whom were not exposed to the chemical. One needs to consider the ways in which the workers might be different from the general population in addition to their exposures at work and utilize tools to control from non-comparability.

22. Not all sources of non-comparability are known.6 Providing that they are not a necessary accompaniment of the variable being investigated, these residual factors are distributed by chance between the two groups being compared. The result is that there are usually differences solely attributable to the random way these factors are distributed between groups in the particular study. The "chance" fluctuations in apparently otherwise similar populations require an epidemiologist to use special tools to discern the true meaning from the chaos of disparate data – to "see" the true picture amidst a welter of images, or to "hear" the true, underlying "signal" in the midst of the noise produced by these variations. The mathematical tools used for these purpose involve statistical analysis.

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6 This is a deterministic view of disease causation. One could also take a probabilistic view, in which case scientists would have to discuss sample error from some assumed super-population of identical study settings. This alternative view does not affect any of the points made

23. The main purpose for statistics in epidemiology, then, is to evaluate the role that random effects ("chance") might have played in the results. Statistical methods do not prove that chance is the source of a difference (or lack of difference). These methods only provide information on how likely it is that chance could have played a part if there were no bias and no true effect. The meaning of "statistical significance" is that the likelihood that chance could have produced the observed results if there were no bias and no real effect is less than some arbitrarily predetermined level, such as 5% ("p<.05").7

24. For the reasons stated above, it is absolutely false – and, indeed, a serious interpretive error – to assert that a result that is not "statistically significant" means the results must be due to chance and only to chance. And for these reasons, prominent epidemiologists eschew "statistical significance," believing that it is not a sine qua non of "good science" and maintaining that "it is neither necessary nor appropriate as a requirement for drawing inferences from epidemiologic data."

25. These views are hardly mine alone. Instead, they are representative of the views of both Sir Austin Bradford Hill, one of the 20th century's preeminent statisticians, and some of most highly regarded epidemiologists in this country, such as Dr. Kenneth Rothman (who is: (a) the co-author of the most widely used textbook on epidemiology; (b) the former Editor-in-Chief of the peer-reviewed journal, Epidemiology; and, not least, (c) my colleague at the Boston University School of Public Health) as well as other epidemiologists, such as Dr. Noel Weiss.

26. Thus, Hill chided those who relied on "significance tests" to prove or disprove causation:

> No formal tests of significance can answer those questions. ("Is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?") Such tests can, and should, remind us of the effects that the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond that they contribute nothing to the 'proof' of our hypothesis." - "I wonder whether the pendulum, has not swung too far -- not only with the attentive pupils, but with the statisticians themselves. - Fortunately I believe we have not yet gone so far as our friends in the USA where, I am told, some editors of journals will return an article because tests of significance have not been applied. . ." 8

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7 The original source of the 5% criterion is lost in time. It apparently came from the original applications of statistical methods to agricultural experiments and expressed a cost-benefit statement about the expense of redoing a large trial involving a whole growing season and plots of various seeds and fertilizers. Its use for public health purposes might thus be questioned. It is interesting to note that in other sciences, notably, physics, another common criterion for "statistical significance" is not 5% but 10%. In any event, virtually every elementary statistics text warns the student of the highly arbitrary nature of the figure.

8 Austin Bradford Hill, The Environment and Disease - Association or Causation? Proceedings of

27. Similarly, in an amicus brief to the US Supreme Court in the Daubert case, Professors Rothman and Weiss, and others including me, stated: "Significance testing, however, is neither necessary nor appropriate as a requirement for drawing inferences from epidemiologic data." [9]

28. The amicus brief continued:

> The notion that only when data demonstrate "statistical significance" do epidemiologists draw inferences about observed associations between suspected risk factors and medical conditions is mistaken. Significance testing is nothing more than a statistical technique that attempts to evaluate what is called "chance" as a possible explanation for a set of observations, and classify the observations "significant" or "not significant" based on the likelihood of observing them if there were no relationship between the suspected cause and effect.

29. Testing for significance, however, is often mistaken for a sine qua non of scientific inference. Scientific inference is the practice of evaluating theories. As such, it is a thoughtful process, requiring thoughtful evaluations of possible explanations for what is being observed. Significance testing, on the other hand, is merely a statistical tool that is frequently, but inappropriately, utilized in the process of developing inferences.

30. Dr. Rothman has stated the issue thus:

> With the focus on statistical significance, if chance seems to be a plausible explanation, then other theories are too readily discarded, regardless of how tenable they may be. As a result, effective new treatments have often been overlooked because their effects were judged to be "not significant," despite an indication of efficacy in the data. Conversely, if "significance" seekers find that the results of a study are calculated as improbable on the basis of chance, then chance is often rejected as an explanation when alternative explanations are even less tenable. 10

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the Royal Society of Medicine (1965) 58: 296 at p. 299.

9 Rothman and Weiss, "Summary of Argument" section of their amicus brief in Daubert.

10 Rothman et al., amicus brief in Daubert, citing K. Rothman, Significance Questing, 105 Annals of Internal Medicine 445, 445-46 (1986) (citations omitted). According to the Rothman-Weiss amicus brief:

A better approach to evaluating the error in scientific measurement is the use of "confidence intervals." A confidence interval is a range of possible values for a parameter that is consistent with the observed data within specified limits. The process of calculating a confidence interval within the chosen limits is know as "interval estimation." See K. Rothman, Significance Testing at 119.

An important advantage of interval estimation is that it: "do[es] not require irrelevant null hypothesis to be set up nor [does it] force a decision about 'significance' to be made -- the estimates can be presented and

31. The outcomes of statistical tests are strongly influenced by the size of the study population. For small populations, very large observed differences, of substantial public health significance, may still not be statistically significant11. That is to say, a large effect that a scientist would take seriously from the public health point of view cannot be differentiated on its face from chance. Either chance or a real causal influence (or bias) could be responsible for the worrisome effect. Conversely, in large populations, very slight and substantively meaningless differences can be "statistically significant."12

32. Statistical methods are sometimes viewed as standard, agreed-upon, and mechanical procedures. Scientists even allow computers to do them, seemingly without human intervention. But as any statistician knows, there is a great deal of judgment in deciding which tests to use in which circumstances, which tests are valid in those circumstances, and what they do and do not mean. Less well recognized is that statistics itself is, like all active disciplines, a field in ferment and change. Thus not all statisticians will agree on the propriety of even commonly used tests13.

33. When used, statistical methods are meant to help scientists evaluate the possible role of chance14. Scientists must evaluate the possibility of a concurrent real effect separately. The most important reason for a difference between two groups, however, is an actual effect or influence from the variable being studied (exposure at work in my

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evaluated by statistical and other criteria, by the researcher or the reader. In addition the estimates of one investigation can be compared with others. While it is often the case that different measurements or methods of investigation or theoretical approaches lead to 'different' results, this is not a disadvantage; these differences reflect important theoretical differences about the meaning of the research and the conclusions to be drawn from it. And it is precisely those differences which are obscured by simply reporting the significance level of the results.

Rothman, et al., amicus brief in Daubert, quoting L. Atkins and D. Jarrett, The Significance of "Significance Tests," in J. Irvine and I. Miles (eds.) Demystifying Social Statistics (1979).

11 A detailed example showing how results can be of public health significance but not statistical significance can be found in Ozonoff, David, "Conceptions and Misconceptions about Human Health Impact Analysis," Environmental Impact Assessment Review, 14:499-516, 1994.

12 For example, a difference of 1/8" in height between east coast children and west coast children will be statistically significant if very large numbers of children on both coasts are measured.

13 A good example is the Fisher Exact Test, commonly used for small tables frequently encountered in environmental epidemiology. Certain well known statistical programs even force the user to employ this test if several table cells contain expected values of less than five, even though it has been known for years that the test is inappropriate. Cf. D'Agostino R, Chase W, Belanger A, "The appropriateness of some common procedures for testing the equality of two independent binomial populations," Am Statistician 42:198-202, 1988, and references therein.

14 As expressed by the epidemiologist Kenneth Rothman in his Daubert amicus brief: "The result of using significance testing as a criterion for decision making is that the focus is changed from the information presented by the observations themselves to conjecture about the role chance could have played in bringing about those observations." [emphasis in original]. Quoted by Berger M, cited above (op. cit., note 8). Rothman is the author of a standard text, Modern Epidemiology (see next note), and former Editor in Chief of the journal Epidemiology.

example), i.e., that "A does cause B." As discussed in greater detail below, scientists recognize that "causation" should not be regarded as an experimental or epidemiological result, but rather as a "judgment" made about the experimental or epidemiological data. See Federal Judicial Center Reference Manual on Scientific Evidence (1994) at p. 157 ("causation is a judgment issue for epidemiologists and others interpreting the epidemiological data."). See also the extended discussion of this point in K. Rothman & S. Greenland, Causation and Causal Inference," in: K. Rothman and S. Greenland, Modern Epidemiology (Second ed. 1997) at pp. 7-2815.

34. It is apparently not always appreciated that this is true. There is a tendency to believe that somehow "causation" is not a subjective judgment or interpretation but an actual, real, objective, discoverable, and measurable property of a relationship that can be demonstrated empirically, as if some associations had readable labels on them that said 'causal' and all that scientists need is the right instrument to read the label.16 In sum, although some scientists may be loathe to admit it, and although many lawyers and judges may not believe it, there is simply no magic formula or easy checklist for making scientific judgments17.

35. The relative risk (RR) or its equivalent (the odds ratio (OR) as an estimate of the relative risk) is itself an estimate from the data of an underlying reality, the "real" risk.

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15 As professors Rothman and Greenland explain, at p. 22 of their textbook:
Perhaps the most important common thread that emerges from the debated philosophies [of scientific causation] is Hume's legacy that proof is impossible in empiric science. This simple fact is especially important to epidemiologists, who often face the criticism that proof is impossible in epidemiology, with the implication that it is possible in other scientific disciplines. Such criticism may stem from a view that experiments are the definitive source of scientific knowledge. Such a view is mistaken. Even the most careful and detailed mechanistic dissection of individual events cannot provide more than associations.

16 Thus Judge Kosinski, in the Daubert remand, writes of the plaintiff's case that it does not "attempt to show causation directly; instead, they rely on experts who present circumstantial proof of causation." Of course there is no such thing as a "direct" proof of causation.

17 Professors Rothman and Greenland are not alone in their view that judgment – not a checklist -- is a scientist's most useful tool in inferring causation. Indeed, that perspective is shared by a number of the nation's leading epidemiologists and other scientists, historians of science, and philosophers of science. Thus, an amicus brief tendered to the US. Supreme Court in the Daubert case by Harvard professors Stephen Jay Gould (Zoology, Geology, and History of Science), Gerald Holton (Physics and History of Science), Everett Mendelsohn (History of Science), and Kathleen Joy Propert (Biostatistics), Columbia University professor Ronald Bayer (Sociomedical Sciences), and NYU professor Dorothy Nelkin (Sociology and Law) explained that "'[c]onclusiveness in inferring causality -- in epidemiology as with the study of all free-living human beings – is a desire more often than an accomplishment.'" Amicus Brief of Bayer, Gould, etc., quoting Mervyn Susser, Rules for Inference in Epidemiology, 6 Regulatory Toxicology and Pharmacology 116, 127 (1986). These scholars went on to observe that "[a]s a consequence, those who seek in science the immutable truth they find lacking in the law are apt to be disappointed." (Ibid.) Furthermore, "One notable similarity [between law and epidemiology] is the dependence of both fields upon subjective judgments. In the end, a quality which lawyers should understand -- judiciousness -- matters more than any. Scientists use both deductive and inductive inference to sustain the momentum of a continuing process of research. The courts of law, and the courts of application, use inference to reach decisions about what action to take. Those decisions cannot rest on certitudes, most especially when population risks are converted into individual risks." (Ibid., quoting Susser, op. cit., at p. 128 (my italics)).

RRs or ORs, like other statistics used to summarize data, have some margin of uncertainty associated with the fact that the data are in some sense just one realization of an idealized, very large set of possible realizations, just as the results of flipping a fair coin ten times varies from one realization (set of ten flips) to the next. Thus the RR or OR has a "confidence interval" around it that expresses how "stable" the estimate is in repeated trials.

36. A RR = 1.7 is a summary of the overall risk to a population that is usually heterogeneous with respect to important risk factors. Thus it might include smokers, alcoholics, people who are obese, the point has been made repeatedly in the literature, accompanied with graphic examples of how a study that produces a RR less than 2.0 could result from an exposure in which all of the cases, some of the cases, or none of the cases were the result of exposure.

37. There is often disagreement among experts, stemming from differing weights each places on the influence of bias, chance and real effect. Such differences in science are common, both in and out of court. The fact that two scientists have different judgments about how much weight to give a study does not demonstrate that either has failed to use scientifically acceptable reasoning, but only that the ultimate opinion about the weight to accord a study is inherently part of the subjective judgment process of scientists.

38. Because there are no fixed, definite, and generally agreed upon rules about how -- and how far -- to generalize, each study must be evaluated in a specific context. Certain generic questions arise frequently, such as how much weight to put on experimental studies in animals, in the absence of definitive human studies, or how does a scientist reach a conclusion about the biological plausibility of a relationship between an exposure and a disease in humans.

39. How does a scientist legitimately assert that such a generalization is valid and reliable? In essence scientists put forth reasons why such a generalization makes sense, for example, that the experimental results in animal studies are relevant to humans, followed by an examination of reasons that might limit the generalization, for example, that the high doses used may alter the process sufficiently that it no longer applies to human exposures.18 Defining and constraining generalizations is an active process for forming opinions about studies. Again, there is ample scope for shades of opinion among experts who devote their professional time, resources, and best efforts to these areas of inquiry.

40. Arriving at an Explanation: Assembling the Picture. Clinical observations and case reports, epidemiological and animal studies, and toxicological experiments are like the pieces of picture puzzle, albeit with the difference that the pieces are being fit into a

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18 It should be noted here that high dose animal studies are generally accepted by scientists and regulators. Cf., for example, Huff, et al.., "Carcinogenesis studies: Results of 398 experiments in 104 chemicals from the US National Toxicology Program", Ann NY Acad Sci 534:1-30, 1988. Cf. also, Reference Guide on Toxicology, pp. 190- 191.

picture that is being formed in the mind of the scientist on the basis of, and at the same time, that the individual pieces are being discovered and taking shape, and with additional caveats that some existing pieces may not fit (and thus may not be used) and that not all of the pieces that might be needed to fill in the picture are available for placement in the picture when the scientist completes the process, let alone when he or she starts the process. All in all, fitting the pieces into a scientific picture is a fluid, dynamic, and difficult process.

41. Depending upon a scientist's judgment of the internal validity (or inherent quality) of a particular study, an individual "piece" may be clear and well defined, or fuzzy and indefinite. Depending upon a scientist's judgment of external validity of a particular study, he or she may decide that an individual piece forms a large and central part of the picture, or is just a small piece on the periphery of the picture, or not even part of the picture at all19. In addition, a scientist's experience, expertise and basic judgment are involved.

42. The objective for the scientist is to take the available picture pieces, judge their internal and external validity, and assemble a picture (a theory or working diagnosis), that uses the majority of the clear and definite (i.e., internally valid) and the most relevant (i.e., externally valid) pieces into a coherent, sensible, comprehensive, and "elegant" picture of "reality," i.e., a picture that represents his or her decision about "what is happening."20

43. In such a complex process and with practical matters of consequence at stake, it is not surprising that differences of opinion develop. It is also not surprising that such differences are highlighted and, indeed, magnified by the adversary process. But even when so magnified, such disagreements are not merely artifacts of the adversary process, but actually essential features of science as it is routinely practiced rather than evidence of flawed scientific reasoning or methodology.

44. In sum, scientists may (and often do) disagree about which pieces are internally valid (which ones can be used in putting together a picture), disagree about which pieces are externally valid (relevant and suitable for fitting into the picture), and disagree about where each internally and externally valid piece should go, that is, just how to assemble the relevant pieces of the puzzle. What scientists do not disagree about, though, is that they routinely select pieces and assemble such pictures and call the end product of this process of selection and assembly an explanation.

45. In this matter, Dr. Dean Hashimoto has reviewed Mr. Dan Allen's medical history and the various epidemiologic studies listed in his report. He gives relatively little attention to the studies regarding chemical exposures and the development of amyotrophic lateral sclerosis (ALS) and he notes the absence of a "statistically significant

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19 External and internal validity are thus analogous to the "reliability" and "fit" criteria of the Daubert Court.

20 See Kuhn, op cit.

association" between solvents and ALS in some of the studies and concludes that it is more likely than not that Mr. Allen's disease was not caused by solvent exposure. Dr. Hashimoto does not discuss other important information such as plausible biologic mechanisms of neurologic damage from solvents, exposure-related symptoms Mr. Allen experienced at the time of the re-surfacing, and case reports of solvent-exposed individuals in the scientific literature. He has therefore failed to take into account the full range of relevant information that is available before reaching his conclusion.

46. Dr. Marcia Ratner provides an extensive review of the neurological mechanisms by which chemicals, including toluene, might cause or contribute to the development of ALS. She also reviews Mr. Allen's medical history, his symptoms and their similarity to case reports of workers exposed to greater than 600 parts per million of toluene. She further reviews the available epidemiological literature, including a study by McGuire, et al. (1997) which she notes found an increased risk of ALS in those exposed to solvents.

47. Dr. Ratner concludes that the combined evidence from animal studies, case reports, mechanistic evidence, and epidemiologic investigations of the causes of ALS supports her opinion that Mr. Allen would have been unlikely to develop overt symptoms and die of ALS in 2004 had he not been exposed to the chemicals used in the gym floor refurbishment process where he worked.

48. The scientific method followed by Dr. Ratner is more detailed and comprehensive and therefore more appropriate in rendering her opinion than Dr. Hashimoto's method as represented in their two reports in this matter. She has considered and presented the full range of relevant information in forming her opinion.

I hold all of the opinions in this report to a reasonable degree of scientific certainty. I reserve the right to further supplement this report and respond to the reports submitted by the defense.

Signed at Boston, MA on July 23, 2007.

Richard W. Clapp

Richard W. Clapp, D.Sc., MPH

(electronic image of signature with permission)

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May 24, 2007

Michael Mahoney, Esq.
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Re: Laura Allen v. Martin Surfacing

Dear Mr. Mahoney:

You requested that I review the materials which you provided as described in your letter dated March 29, 2007. In addition, I have review the material safety data sheets which you provided me on May 8, 2007. I summarize below pertinent portions of this material. Mr. Daniel Allen was reportedly exposed to solvent odors and vapors because he worked in an office next door to a gym. The gym's floor was refinished. You asked me to provide my medical opinion regarding whether Mr. Allen's exposure to solvent odors and vapors from the refinishing of the gym floor caused him months later to develop amyotrophic lateral sclerosis (ALS).

Medical Records:

Dr. James Russell evaluated Mr. Allen in a neurology clinic at the Lahey Clinic on 1/22/02. Mr. Allen reported noticing twitching of the thighs and right shoulder in August 2001. No functional impairment at this time. CPK elevated at 511. TSH is mildly elevated at 5.76. His occupation is football coach. No other occupational or environmental exposure history is described. No family history of motor neuron disease. He has widespread fasiculations and left foot drop. On follow-up visit on 2/18/02, symptoms are reported as unchanged. The impression is probable motor neuron disease. Dr. Russell did not describe any connection between Mr. Allen's exposure to gym floor refinishing solvents and the development of motor neuron disease.

Dr. David Chad, a neurology professor at UMass Memorial wrote a letter dated 1/28/02. He reports seeing Mr. Allen in clinic that day. He enjoyed excellent health apart from mild hypertension controlled on Zestril. He reported noticing muscle twitching in the past 5-6 months. Mr. Allen reported that in June 2001 the field house floor was redone and that he was sickened by a noxious odor from the building. He felt nausea and dizzy for a few days. He reportedly recovered and then in July took a trip to Aruba where he thought he acquired an infection causing vomiting and diarrhea. He was treated with Cipro for the presumed infection, although it was not definitely diagnosed.

Dr. Chad reported that apart from the exposure to the refinished floor in the field house that there was no definite history of exposure to any known neurotoxic agent or heavy metal. Electrodiagnostic studies point to a disorder of the motor neurons or motor roots. He concludes that ALS was a diagnostic consideration but could not be shown conclusively at that time. He ordered additional tests including a urine collection for heavy metal intoxication, lyme serology, CSF examination, and MRI scan of cervical spine. He started treatment with rilutek.

Lahey Clinic records include a EMG/NCS report from 1/22/02 indicating widespread fasciculations and findings of chronic denervation and reinnervation. A neurology office note states that twitching in thighs and right shoulder were first noticed by Mr. Allen in August 2001. Dr. Russell's office note dated 2/18/02 indicated no interval change and that Mr. Smith wishes to continue to work.

A letter by Drs. George Zabrecky and Marcie Wolinsky-Friedland dated 4/23/03 summarizes office visit on 4/15/03. Initial symptoms in late May or early June 2001 included headache, nausea, lightheadedness, and dizziness. His exposure was approximately one week during which he remained in the enclosed building form the majority of the day. The gymnasium floor was chemically stripped and resealed. His symptoms improved during the summer hiatus. Upon his return to working in his office in August, the symptoms of headache, dizziness and lightheadedness returned. Muscular fasiculations developed in September. Drs. Zabrecky and Wolinsky state that this historical account suggests a primary chemical exposure, inducing injury to the blood brain barrier and immune sensitization. They obtained specific testing including a positive d-glucaric/mercapturic acid test, markers for exposure to toxic compounds, elevated antibodies to his central and peripheral nervous system, and elevated neurofiliment antibodies. They conclude that this testing supports a toxic or xenobiotic exposure that damaged his protective blood brain barrier and induced upregulations of his neuronal immune system.

Dr. Wolinsky wrote a letter dated 2/11/04 indicating that she saw Mr. Allen on 12/22/03 and that he traveled to a clinic in the Bahamas to receive stem cell infusion in an effort to regenerate nerve tissue. She is contemplating treatment with hyperbaric oxygen. Dr. Zabrecky's letter dated 4/18/04 states that a test called Elisa/ACT test showed immune hypersensitivity to several chemicals. Once chemical sensitization occurs, the sensitized cells enjoy a level of immortality and memory to the reactants. According to Dr. Zabrecky, the test establishes his progressive neurological damage to an immune system dysfunction due to an environmental chemical exposure.

Dr. Joe Jabre, a neurologist at Boston University, evaluated Mr. Allen on 4/13/04. Mr. Allen worked in an office adjacent to a gym. The gym's floor was refinished during one work week. Mr. Allen experienced dizziness, headaches, and disorientation. Other people in the area had similar symptoms. One month later, he experienced diarrhea while on a vacation which improved spontaneously. He experienced headaches and dizziness when he returned to work although no further work had been performed on the gym floor. He experienced fatigue and weakness that was treated with Paxil. In September 2001, he

developed fasiculations in the lower extremities that spread to his arms. He became wheelchair bound in the spring 2003. He has hypothyroidism. Dr. Jabre acknowledges that "studies looking at tan association between the prevalence or incidence of ALS have failed to find a significant association between exposure to any specific neurotoxic chemical and the occurrence of the disease" and that "the association between neurotoxic chemical exposure history and age at onset of ALS which is more likely to occur has not been as extensively studied." However, he concludes "it is impossible for us to exclude the role of exposure to neurotoxic chemicals in the onset or progression of ALS and ultimately to the untimely death on May 16, 2004 of the patient in this case" He also concludes that "there is sufficient evidence to support the conclusion that the exposure was a major contributory factor since there was no reported family history of the disease, the age at onset was atypical, the onset occurred after the exposure event, and several of the chemicals Coach Allen was exposed to are known to be neurotoxic (e.g., toluene)." Finally, he concludes, "It is therefore our conclusion with a reasonable degree of medical certainty that Coach Allen would have been unlikely to develop overt symptoms of ALS at age 45 years old and would not have died on May 16, 2004 had he not been exposed to the chemicals used in the gym floor refurbishment process."

Dr. Alexander Chirkov, a pathologist, wrote a letter dated 1/03/05. He concludes that the clinical lab studies failed to classify the disease. He points to clinical lab studies including elevated antibodies to his central and peripheral neurosystem, elevated microfilament antibodies, and no specific clinical picture of the disease "give basis for assumption of the initiation of the disease by toxic exposure." He acknowledges, however, that "Absence of direct information about chemical used in remodeling of Gymnasium floor and roof makes it difficult to point to direct relationship between the exposure and the disease...." He then describes various solvents and chemicals used in this type of work as toxic and hazardous.

The material safety data sheets (MSDS) contain descriptions of chemicals associated with Martin Surfacing products. They describe organic solvents including Polyoxy Propyleneglycol, Aromatic Isocyanate Prepolymer (MDI), xylene, ethyl benzene, toluene, ethanol, 2-butanone, toluene, methylene chloride, and other solvents. The typical symptoms from inhalation include headache, dizziness, and nausea. In high doses and through direct contact, there may be central nervous system depression. The MSDS do not indicate that any of the solvents or other substances cause ALS or other chronic neurodegenerative disease.

The death certificate for Mr. Allen is dated 5/16/04. The cause of death is listed as neuromuscular degeneration. No autopsy was performed.

Medical Literature:

There are no published peer-reviewed studies that have evaluated the relationship between indoor air quality exposures to solvent vapors and ALS. No medical research has studied the type, duration, or quantity of exposure to solvents experienced by Mr.

Allen. His exposure was limited to less than one week in duration. He did not have direct contact with the solvents. His office was next door to the gym.

Published studies have evaluated various factors that may be associated with ALS. However, the medical consensus is that medical science does not yet have enough data to make a determination that any single factor is the cause of ALS. The factors identified by published studies have not been consistently found to be associated but they include physical trauma, engagement in competitive sports, thyroid disease, infections, pesticides, contact with animals, heavy metals, lower socioeconomic class, living in rural areas, and other factors. It is notable that Mr. Allen may have had a significant history of exposure to physical trauma, engagement in competitive sports, thyroid disease, and infections. But it is impossible to know if any of these factors is the "cause" of his ALS. Even when an association is found by some studies with one or more of these factors, medical experts have not determined that the association is causal. This is because the results are inconsistent; there is the possibility of significant confounding; there is often a lack of sufficient numbers; the studies are usually retrospective and may have selection bias; the exposure information is crude and uncertain; as well as other analytic issues. This is consistent with the consensus scientific perspective that sporadic ALS is of unknown etiology that is probably the result of many yet to be identified causes.

Some studies are mixed with respect to finding an association between solvent exposures and ALS.

Argyriou et al (2005) evaluated 133 ALS patients in southeast Europe. No potentially causative clinical associations were found and no relationship between occupational exposure and disease were noted. The study authors note that the causes of ALS is presently unknown.

Savettieri et al (1991) conducted a retrospective case-control study using 42 patients with ALS and 92 closely matched healthy controls. No statistically significant association was found between ALS and a number of possible risk factors including organic solvents.

McGuire et al (1997) studied 174 cases of newly diagnosed ALS were matched with 348 controls. Four industrial hygienists blindly assessed detailed lifetime job histories for exposures to solvents, metals and agricultural chemicals. Based on the panel's assessment, overall exposure to solvents for men and women combined was not significantly associated with ALS. Specific solvent exposures associated with ALS were alcohol and ketones, benzene, toluene, and xylene, and cleaning solvents and degreasers, although no dose-response trends were found. The authors of this study concluded that even in instances where there were associations found, the results should be considered exploratory and not confirmatory.

Kondo and Tsubaki (1981) published two case-control studies of motor neuron disease that involved 712 cases and 158 cases. No association was found between ALS and exposures to chemicals. While they found an association between ALS and mechanical trauma, the authors were careful in noting that causation was not established.

Deapen and Henderson (1986) conducted a study of 518 ALS patients and 518 controls. Occupational exposures to selected toxic substances was similar for ALS patients and controls except for the manufacture of plastics, although few details of these exposures was provided.

Other studies have found exposure to solvents to be associated with ALS, such as Chio et al (1991) and Gunnarsson et al (1992). However, none of these studies focused on indoor air quality exposures to solvent vapors or identified short-term exposures of less than one week duration. Despite identifying positive associations, Chio et al (2002) recognize the medical consensus viewpoint that the cause of ALS is unknown.

Assessment:

Mr. Allen had sporadic (idiopathic) amyotrophic lateral sclerosis (ALS) based on clinical history, EMG/NCS, normal CSF analysis, negative heavy metal 24-hour urine screen, and negative imaging studies. The etiology of sporadic ALS is idiopathic (unknown). The only established risks of sporadic ALS are age and male gender.

Mr. Allen's occupational and environmental history was not obtained in sufficient detail by the physicians who evaluated him. There is no detailed list of his past jobs or hobbies. Nor is there detailed listing of his exposures to physical trauma, infections, or other solvent exposures.

Mr. Allen's exposure to solvents associated with the refinishing of the gymnasium floor is properly characterized as indirect and of short duration in comparison to the solvent exposures that scientific researchers have chosen to evaluate in peer-reviewed medical literature. There is no peer-review published study that has examined the indirect and limited exposure reported by Mr. Allen. Instead, the published studies have evaluated occupational exposures of substantially greater duration where the potential exposure is from direct and sustained contact with the solvents.

It is my medical opinion, based on reasonable medical certainty, that Mr. Allen's medical condition of ALS was not caused by his exposure to the refinishing materials used on the gymnasium floor. Current medical science has not established that organic solvents cause or initiate ALS. Scientific researchers have not established any relationship between ALS and the indirect and limited duration of exposure to solvents odors and vapors that may result from refinishing a gymnasium floor.

Sincerely yours,

Dean Hashimoto, M.D.

Dean M. Hashimoto, M.D.
Chief of Occupational and Environmental Medicine
Massachusetts General Hospital / Brigham & Women's Hospital
Partners HealthCare System
101 Merrimac Street, 4th Floor
Boston, MA 02114

October 15, 2007

Michael Mahoney, Esq.
Mullen & McGourty
52 Temple Place, 4th Floor
Boston, MA 02111

Re: Laura Allen v. Martin Surfacing

Dear Mr. Mahoney:

I appreciate this opportunity to clarify the medical opinion I provided in my letter dated May 29, 2007. I wish to provide a more detailed explanation of four issues that were discussed in my letter.

First, it is my professional opinion, based on reasonable medical certainty, that Mr. Allen's medical condition of ALS was not caused by his indirect, one-week duration exposure to the refinishing materials used on the gymnasium floor. By this statement, I mean that the refinishing solvents did not cause or hasten the onset or progression of ALS. As I indicated in my letter, current medical science has not established that organic solvents cause or initiate the onset of ALS.

Second, my reference to the medical scientific literature encompasses epidemiological, animal, and other laboratory research. This current medical science has not established that organic solvents cause or hasten the onset or progression of ALS. A reference given by one of the plaintiff's experts, Dr. Christine Oliver,` is a well-known medical textbook reference on neurology that describes the ALS animal and laboratory research involving the enzyme superoxide dismutase, excess in free radicals, and glutaminergic activity. It concludes that while this research approach is provocative, it is "unknown" whether these enzymatic and biochemical abnormalities in fact extend to the sporadic type of ALS. It concludes that the "pathogenesis of sporadic motor system disease is not known."*

Third, I previously pointed out that Mr. Allen's exposure history was not obtained in sufficient detail and that the published ALS studies have evaluated occupational exposures of substantially greater duration where the potential exposure is from direct and sustained contact with the solvents. The plaintiff's experts have attempted to

* Adams and Victor's Principles of Neurology (7th ed.), pp. 1157-58.

characterize Mr. Allen's exposure as being a "toxic" exposure based on his reported symptoms including dizziness, headaches, nausea, and disorientation. However, there are no objective measurements of Mr. Allen's actual exposure. We do not know the amount of toluene or other organic solvents that Mr. Allen was exposed to. His reported symptoms are more likely to have been caused by mucous membrane irritation or by odors associated with the indirect exposures to low amounts of solvent mixtures in an indoor office setting.

Finally, it is quite striking that there are no published peer-reviewed studies that have established that organic solvents, including toluene, cause or hasten the progression of ALS. As a result, the medical and scientific community does not generally accept the viewpoint that organic solvents, including toluene, cause or hasten the progression of ALS. There is a lack of logically reliable scientific information demonstrating a causal connection between organic solvents and ALS. There is no peer-reviewed ALS study that has examined the indirect and limited exposure to solvents reported by Mr. Allen. Generally, the assessment of the degree of solvent exposures in ALS studies lack accuracy and are not relevant to indirect and short-term solvent exposures. There is a lack of consistency in finding statistical significance in ALS studies that evaluate the association between ALS and organic solvents. Our knowledge of the pathogenesis of ALS is quite incomplete. There are many potential confounding factors that are not accounted for in ALS epidemiological studies

In summary, current medical science has not established a causal relationship, including the initiation or hastening of the onset, of ALS by the indirect and limited duration of exposures to solvent vapors and odors experienced by Mr. Allen while working in an office next door to where there was a refinishing of a gymnasium floor.

Very truly yours,

Dean Hashimoto

Dean Hashimoto, M.D.

References:

Hodgson MJ and Addorisio MR, *Exposures in Indoor Environments,* in Rosenstock L, Cullen MR, Brodkin CA, and Redlich CA, Textbook of Occupational and Environmental Medicine (Elsevier Saunders 2005), 1133-1142.

Monson RR, Occupational Epidemiology (CRC Press 1990), 87-101.

Toxicological Profile for Toluene, Agency for Toxic Substances and Disease Registry (U.S. Dept. of HHS).

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION NO. 05-40048-FDS

AFFIDAVIT OF PAUL BACHIA

I, Paul Bachia, do hereby depose and state as follows:

1. My name is Paul Bachia.

2. I offer the following based upon my personal knowledge and to the best of my memory.

3. As of May, 2001, I was the Running Backs Coach and recruiting coordinator for the men's football program at The College of the Holy Cross in Worcester, Massachusetts, reporting to Coach Allen.

4. As of May, 2001, my office was located in the "Field House" on the Holy Cross campus. Coach Allen worked in the Field House as well, on the same floor. My office was directly across from Coach Allen's office.

5. In late May/early June 2001, a crew of workers re-surfaced a new athletic floor on the first level of the Field House (our offices were located on the second level).

6. Prior to the appearance of the work crew, I was told by the College only that the Field House floor was being resurfaced, and to stay away from the Field House if I did not have to be working in the building.

7. I was not told by anyone about any risks or hazards of any chemicals used by the workers. To my memory, there were no posted warnings about any such risk or hazard.

8. The resurfacing was conducted approximately ten yards below my office.

9. Coach Allen was present in the building during the re-surfacing work. His office was also just about 10 yards away from the work below.

10. The workers performed this re-surfacing for approximately two weeks.

11. I saw the workers performing the re-surfacing work, and recall saying "hello" to them whenever I did see them.

12. During the re-surfacing work, I smelled and felt the effect of the fumes from the chemicals being used by the workers: I felt a burning sensation in my eyes and, when I breathed deeply, I felt a burning sensation in my throat. I also felt light-headed during the weeks of the re-surfacing work, as I actually slept overnight in this building during the week.

13. No one ever told me not to work or sleep in the building.

14. I personally observed Coach Allen as light-headed and nauseous during the re-surfacing work.

SIGNED THIS 19 DAY OF MAY, 2007 UNDER THE PENALTIES OF PERJURY.

Paul T. Bachia

Paul Bachia

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION NO. 05-40048-FDS

AFFIDAVIT OF ROBERT BRADLEY

I, Robert Bradley, do hereby depose and state as follows:

1. My name is Bob Bradley.
2. I offer the following based upon my personal knowledge and to the best of my memory.
3. As of May, 2001, I had known Dan Allen (we referred to him as "Coach Allen") for approximately 18 years.
4. As of May, 2001, I was an assistant football coach at The College of the Holy Cross in Worcester, Massachusetts, reporting to Coach Allen.

5. As of May, 2001, my office was located in the "Field House" on the Holy Cross campus. Coach Allen worked in the Field House as well, on the same floor and only approximately 10 yards from my office.

6. In late May/early June 2001, a crew of workers re-surfaced a new athletic floor on the first level of the Field House (our offices were located on the second level).

7. I was present during the course of this work. Coach Allen and his assistants were preparing for the Coach's annual Football Camp, which was scheduled to begin just after the completion of the floor re-surfacing. Our preparations required much organization and data entry (i.e. we had to register the campers, assign them to their respective groups, check for insurance coverage, check for medical clearance, make sure gear was available, etc.). Most of the data was entered into the office computer in the Field House.

8. Prior to the appearance of the work crew, we were told by the College only that the Field House floor was being resurfaced. We were not told about any risks or hazards of any chemicals used by the workers. There were no warnings posted at the Field House to my recollection. No one asked or instructed me to stay away from the Field House.

9. The workers did not provide any warnings or instructions to me or, to my knowledge, anyone else working inside the Field House.

10. To my memory, the workers wore at least protective masks during the entire resurfacing.

11. The resurfacing was conducted approximately ten yards below our offices.

12. I recall the weather during this period was hot and humid.

13. I recall that the air conditioning was operating during the work, so our office windows would have been closed.

14. No ventilation system was set up or used by the workers to address the fumes created by their chemicals.

15. During the re-surfacing work, I smelled and felt the effect of the fumes from the chemicals being used by the workers: the fumes were noxious; I felt dizzy and suffered headaches throughout this period.

16. I observed that the other assistant coaches were similarly affected.

17. None of the coaches would linger at the Field House during the construction. As soon as our work was completed, we left immediately. I recall my wife picking me one day during this period. She stayed inside the Field House for two minutes and ran out in response to the fumes; she suffered a headache for more than a day.

18. I personally observed that Coach Allen was similarly affected. He was known as someone who hates to complain, but he was visibly dizzy.

19. In the weeks before the re-surfacing work, Coach Allen appeared perfectly healthy to me.

20. Because the data entry needed to be completed in order to begin his camp, he stayed longer than any of us. Coach Allen allowed his assistants and staff to leave early, but he stayed to complete the preparations for camp.

SIGNED THIS 18 DAY OF MAY, 2007 UNDER THE PENALTIES OF PERJURY.

Robert Bradley

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION NO. 05-40048-FDS

AFFIDAVIT OF LARRY NAPOLITANO

I, Larry Napolitano, do hereby depose and state as follows:

1. My name is Larry Napolitano.
2. I offer the following based upon my personal knowledge and to the best of my memory.
3. As of May, 2001, I was the coordinator of athletic media relations for Holy Cross College and then became the director of athletic media relations in July of 2001.
4. My office was on the ground floor of the Field House, across from Coach Dan Allen's office.

5. I was present during the entire floor re-surfacing of the Field House in May-June 2001.

6. Prior to the commencement of the re-surfacing work, I don't think I knew anything about it. I just came to work that first day, smelled an awful smell and realized that they were doing the floor.

7. I recall that the workers were wearing regular clothes, gloves and what appeared to be re-breather masks. They also placed "caution" tape up around the floor so we wouldn't step on it.

8. In relation to my office, since I was on the ground floor, the workers were right outside my office door at one point. They were directly underneath Coach Allen's office.

9. I know the workers saw us because I had to walk through the gym to get to the main office from my office. I have no doubt they knew we were there.

10. I do not recall the outside temperature for the period the workers were present, but it was usually pretty warm in the Field House.

11. I do not think most windows in the building were capable of opening due to the age of the building; I could, however, open my windows.

12. The air conditioner was running in my office and the other offices but the main area of the Field House (where the floor was being re-surfaced) was not air-conditioned.

13. I was physically affected by the chemicals being used during the re-surfacing work. I would get headaches and wave upon wave of nausea. The headaches I remember the most, because they were just absolutely pounding. Every time

I walked into the building the headaches would come back, and the nausea was ridiculous. I have never had headaches that bad (and I have had at least two concussions in my athletic career).

14. Coach Allen was similarly affected, as was everyone else. The smell just permeated everything and with the heat rising to the top of the building it was just worse and worse every day. I could tell it was worse where Coach Allen was located, when I would go up and see him. At least I could open my windows to the outside. He could not open his windows.

15. Coach Allen and I talked during the re-surfacing about how awful it was and how bad the headaches were. I just wanted to go home but couldn't because I had so much work to do. Coach Allen was in the same boat.

16. I do not recall anyone asking, suggesting or instructing me to stay away from the Field House during the installation, and I saw no such warnings posted at the Field House building.

17. I did not see any written warnings posted at the building about the nature of the chemicals being used (i.e. that they were hazardous).

18. Coach Allen looked to be in great physical shape before the re-surfacing work. His contract was extended after the football team went 7-4 in 2000, and we were a very young but talented football team. The future looked very bright.

19. After the re-surfacing work was finished, Coach Allen looked to be in much worse condition. It was the first game in 2001 when I noticed him walking with a limp and slowly working his way to the sidelines at Georgetown. It is an image that I will never forget; I thought he had done something to his leg or knee.

SIGNED THIS 10 DAY OF MAY, 2007 UNDER THE PENALTIES OF PERJURY.

Larry Napolitano

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN, **Plaintiffs,**	
v.	**CIVIL ACTION NO. 05-40048-FDS**
MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING, **Defendants.**	

AFFIDAVIT OF PAUL CRECELIUS

I, Paul Crecelius, do hereby depose and state as follows:

1. I live at 19 Baker Circle in Fryeburg, Maine.
2. I offer the following to the best of my memory and based upon information known personally to me.
3. I worked for Martin Surfacing for approximately nine years.
4. I was one of the employees of Martin Surfacing involved in the installation of a "Versaturf" floor inside the Fieldhouse at Holy Cross College, Worcester, Massachusetts, between May and June 2001.
5. I remember the job at Holy Cross involved the resurfacing of an existing floor. I believe it was an existing Martin floor that was installed well before I started working for the company. The floor was worn out in spots and required resurfacing.

6. As to the process for the resurfacing:
    a. First sanding was done using a Ryder Sander to rough up the floor;
    b. The floor is then cleaned and vacuumed;
    c. After the floor is cleaned, the existing floor is sprayed with a primer (it generally takes four hours or possibly overnight for the primer to dry);
    d. Protective gear is worn by the installers during the spraying (we use a full face organic filter respirator, to filter out organic matters);
    e. After the primer is dried, a resin coating approximately an eighth of an inch thick is applied to the floor (it's a polyurethane rubberized product).
7. We typically seal the door entrances to the work area with plastic.
8. I remember most of the doors leading into the jobsite were exterior doors, and two of the doors led into the main hallway which led into the main lobby area. These two doors were polyed (covered with plastic) to keep out onlookers.
9. I do not believe that there were any operable windows on the ground level of the Field House.
10. The floor is then spray-painted to the desired color.
11. After the floor was dry, we used a large industrial fan to blow the fumes out of the work area. We used one fan that's four foot in diameter.
12. During the process of allowing the floor to dry, there cannot be any air movement. Nothing is turned on until after the entire process. Once the floor is dry, the exhaust system, if there is one, is turned on. If the field house had air conditioning and/or heat, it would not be turned on. Again, nothing is used to disturb the floor before or during the drying process.
13. Any game lines are then laid out and painted by roller.

14. The office at Martin Surfacing typically notifies the customer about any precautions that need to be taken by the school. This is done at the time of the contract.

15. I only vaguely recall that Holy Cross college put up signs about the gym being off limits due to resurfacing, or words to that effect.

16. It's not typical for the installers to put up warnings to vacate and/or a warning about the chemicals being used. If for whatever reason the school did not post warnings, the installers may post a hand written sign warning, to the effect that the floor is being resurfaced and "no admittance", or words to that effect.

17. No warnings were posted on site that the chemicals we used may be hazardous. Datasheets are provided to the customer by Martin's office and available on site during installation; materials on site are labeled as well.

Signed this 11 day of May, 2007, under the penalties of perjury.

Paul Crecelius